State of the art paper

Spontaneous avulsion of the inferior mesenteric artery in a neurofibromatosis type 1 patient: a case-based review

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Submitted: 22 January 2025; **Accepted:** 12 May 2025
Online publication: 2 June 2025

Arch Med Sci Atheroscler Dis 2025; 10: e48–e68
DOI: https://doi.org/10.5114/amsad/205022

Abstract

We present the case of successful endovascular abdominal aortic aneurysm repair (EVAR) in a 55-year-old male who presented with a ruptured infrarenal aortic pseudoaneurysm, formed after spontaneous avulsion of the inferior mesenteric artery. The avulsion occurred after lifting a heavy object. Although aortic endografting is not the first option in patients with hereditary disorders due to aortic friability and concerns about long-term durability, it is valuable in urgent cases due to lower morbidity and mortality, even as a bridging procedure. This policy is further supported by the fact that the alternative open reconstruction has been invariably associated with hemostasis issues and poor outcomes due to arterial fragility and inability to construct safe anastomoses. Finally, we present a current literature review regarding abdominal aortic and iliac pathology in patients with neurofibromatosis type 1 focusing on the type of the vascular lesion, method of repair and outcome.

Key words: endovascular repair, aortic rupture, abdominal aortic aneurysm, neurofibromatosis type 1, von Recklinghausen's disease, iliac aneurysm, iliac rupture.

Introduction

Neurofibromatosis type 1 (NF1) is a heritable disorder involving the central and peripheral nervous system, the skin and soft tissue (neurocutaneous syndrome). The syndrome was also called in the past von Recklinghausen's disease, a term that is no longer recommended by the WHO classification of genetic tumor syndromes [1–3].

Vascular disorders in the setting of NF1 are termed as NF1 vasculopathy. It includes arterial stenoses, aneurysms, dissections, arteriovenous malformations, vascular compression or invasion by neural tumors and spontaneous arterial rupture [1]. They occur at a rate of 0.4% to 6.4% in NF1 patients with most clinical symptoms emerging in the 5th decade of life [1, 4]. Although every artery may be affected, lesions in medium and large arteries predominate with rare aortic involvement [5]. Herein, we present the rare case of a 55-year-old male with NF1 who presented with abdominal aortic rupture and was treated urgently by endovascular abdominal aortic aneurysm repair (EVAR). Additionally, we present a literature review not only with similar cases of abdominal aortic ruptures but with all the aortic and iliac pathology in NF 1. We focus on the type of the vascular lesion, method of repair and outcome. Open repair (OR) and endovascular treatment (ET) each have their own advantages and disadvantages and currently there is uncertainty about which modality is superior. Although endovascular treatment is not suggested in connective tissue disorders, it is currently used in NF1 aortic rupture with acceptable results. While NF1-associated vasculopathy most commonly presents as renal artery stenosis, mid-aortic syndrome, and intracranial aneurysms, spontaneous avulsion of visceral arteries is exceedingly rare. This case adds to the limited number of reports describing NF1-related mesenteric and aortic complications, underlining the need for increased awareness of such unpredictable vascular events.

Case presentation

A 55-year-old male was transferred from a local hospital because of a 3-day persisting and worsening bilateral groin pain along with ultrasound findings of the periaortic mass and fluid. The pain started after lifting a heavy object. He was tachycardic (heart rate: 102 beats per minute) and normotensive (systolic blood pressure: 120 mm Hg), while innumerable neurofibromas and typical café-au-lait spots were noted throughout his face, trunk and upper extremities (Figure 1). His past medical history included arterial hypertension, dyslipidemia and NF1 diagnosed in childhood. He was an active smoker (25 pack years) and he discontinued his medicine (torasemide 2.5 mg o.d., olmesartan medoxomil 20 + 5 mg o.d. and rosuvastatin 10 mg o.d.) 6 months before admission. He had unspecified surgery for a carotid aneurysm 22 years ago. Computed to-

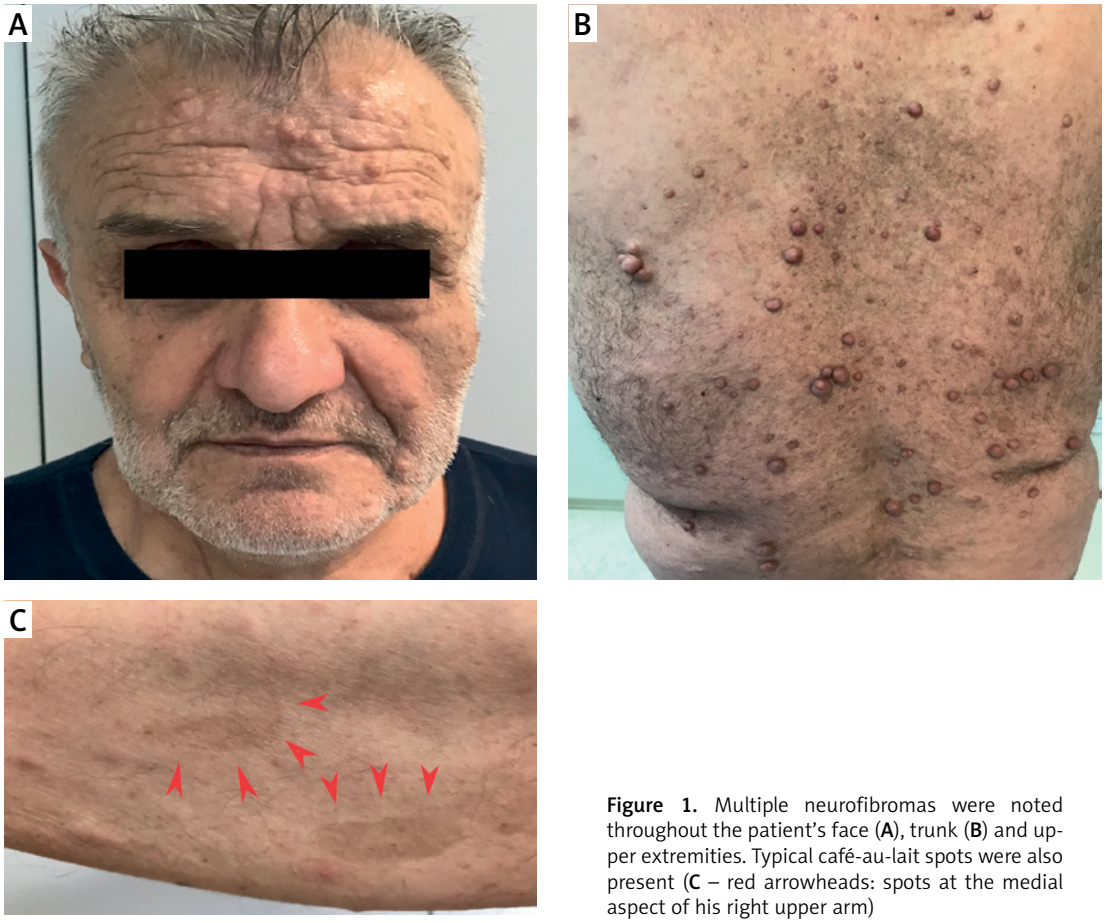

Figure 1. Multiple neurofibromas were noted throughout the patient's face (**A**), trunk (**B**) and upper extremities. Typical café-au-lait spots were also present (**C** – red arrowheads: spots at the medial aspect of his right upper arm)

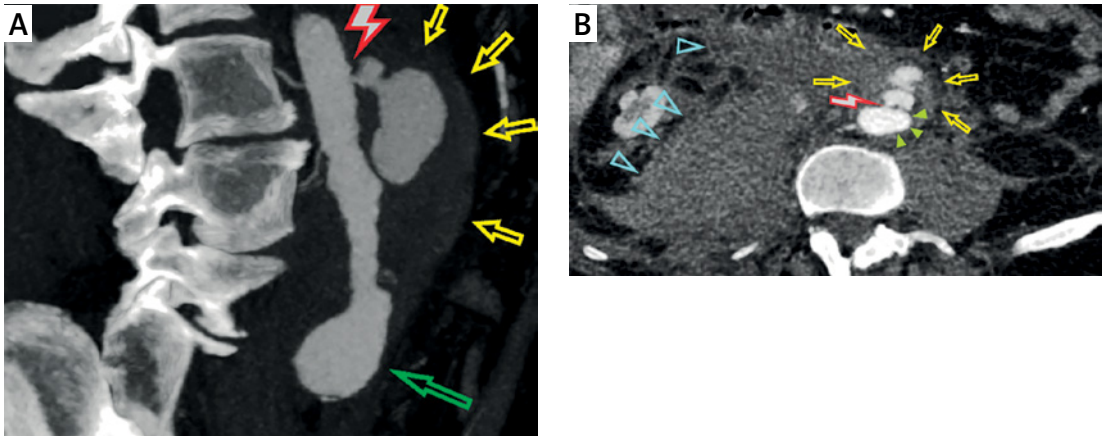

Figure 2. Computed tomography angiography (CTA) revealed an aortic rupture with gross extravasation of contrast media, 3.7 cm below the renal arteries, leading to a pseudoaneurysm and a large retroperitoneal hematoma (**A** – MPR reconstruction, sagittal view: red lightning bolt: aortic rupture, yellow arrows: aortic pseudoaneurysm, green arow: right common iliac artery aneurysm, **B** – Axial view: red lightning bolt: aortic rupture, yellow arrows: aortic pseudoaneurysm, light green arrowheads: focal aortic dilatation, light blue arrows: large retroperitoneal hematoma)

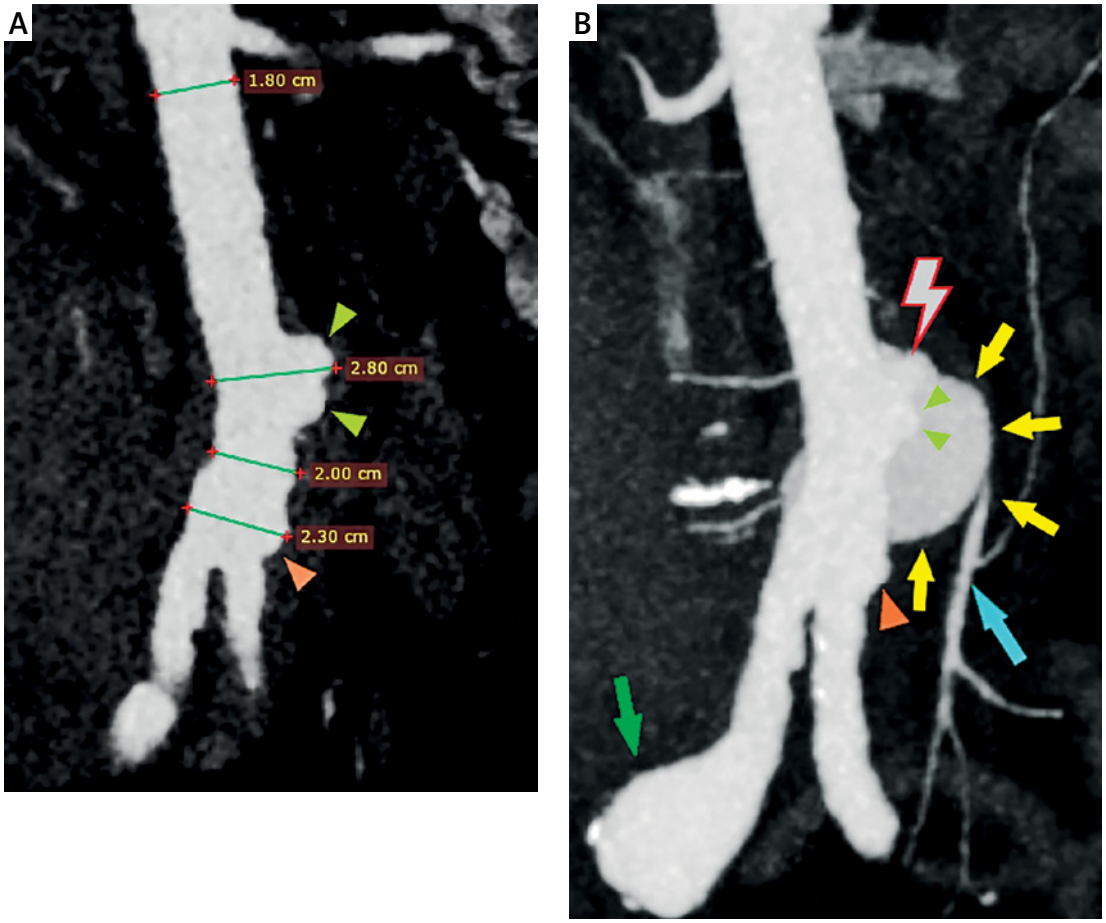

Figure 3. Computed tomography angiography (CTA), MPR reconstruction, coronal view (**A** – light green arrowheads: focal aortic dilatation near the rupture site, orange arrowheads: focal aortic dilatation above the aortic bifurcation), (**B** – red lightning bolt: aortic rupture, red lightning bolt: aortic rupture, light green arrowheads: focal aortic dilatation near the rupture site, orange arrowheads: focal aortic dilatation above the aortic bifurcation, light blue arrow: inferior mesenteric artery, green arow: right common iliac artery aneurysm)

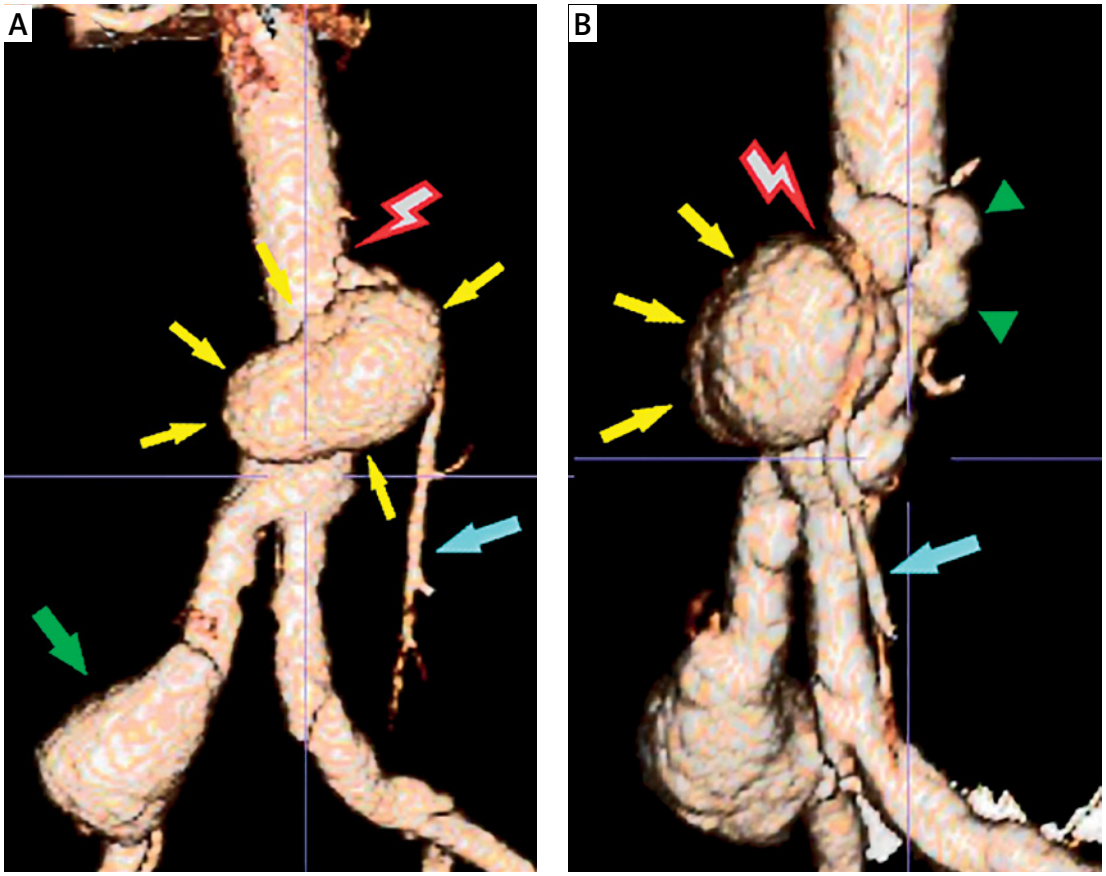

Figure 4. Computed tomography angiography (CTA), 3D-reconstruction (**A** – coronal view: red lightning bolt: aortic rupture due to avulsion of the inferior mesenteric artery, yellow arrows: aortic pseudoaneurysm, green arrow: right common iliac artery aneurysm, light blue arrow: inferior mesenteric artery), (**B** – oblique view: red lightning bolt: aortic rupture due to avulsion of the inferior mesenteric artery, yellow arrows: aortic pseudoaneurysm, green arrowheads: focal aortic dilatation, light blue arrow: inferior mesenteric artery)

mography angiography (CTA) revealed an aortic rupture with gross extravasation of contrast media, 3.7 cm below the renal arteries, leading to a pseudoaneurysm and a large retroperitoneal hematoma (Figure 2). The abdominal aorta was locally ectatic near the rupture site and above the bifurcation; the right common iliac artery (CIA) was 3 cm in diameter (Figures 2, 3). It was obvious that aortic rupture was due to spontaneous avulsion of the inferior mesenteric artery (IMA) (Figure 4). The ascending thoracic aorta was 4 cm in diameter. We proceeded to ET due to concerns for open repair regarding the congenital vascular wall friability and the decreased morbidity and mortality associated with EVAR in ruptured abdominal aortic aneurysms (AAAs) [6]. Anticoagulation was achieved with 2500 units of heparin. A bifurcated endograft (Gore Excluder Conformable Endoprosthesis, W. L. Gore & Associates Inc., Flagstaff, Arizona, USA) was employed through both common femoral arteries cut down and placed infrarenally, after coil embolization of the right internal iliac artery (IIA). The right leg was landed in the external iliac artery (EIA), while the left placed in the CIA. No friability was noted in the common femoral arteries. Carotid duplex ultrasound was normal although the internal carotid artery (ICA) was narrow (2.5 mm in diameter). Brain magnetic resonance angiography revealed chronic obstruction of the petrous part of the ICA. Holter rhythm examination was positive for premature ventricular contractions. He was discharged on the 5th postoperative day (p.d.) in good condition. Follow-up CTA was performed on the 4th p.d., 1st month and 1st year after the operation depicting normal postoperative findings (Figure 5). The ethics committee approval and informed consent have been obtained. This case report was approved by the Institutional Review Board of the University Hospital of Patras (IRB no. 29/11- 07-2018).

Discussion

Clinical presentation of NF1

Neurofibromatosis type 1 is a rare congenital disorder with an autosomal dominant inheritance. It occurs in 1 of 3,000 births and is the most common subtype of neurofibromatosis. It is caused by genetic defects in the NF1 gene, which impairs the

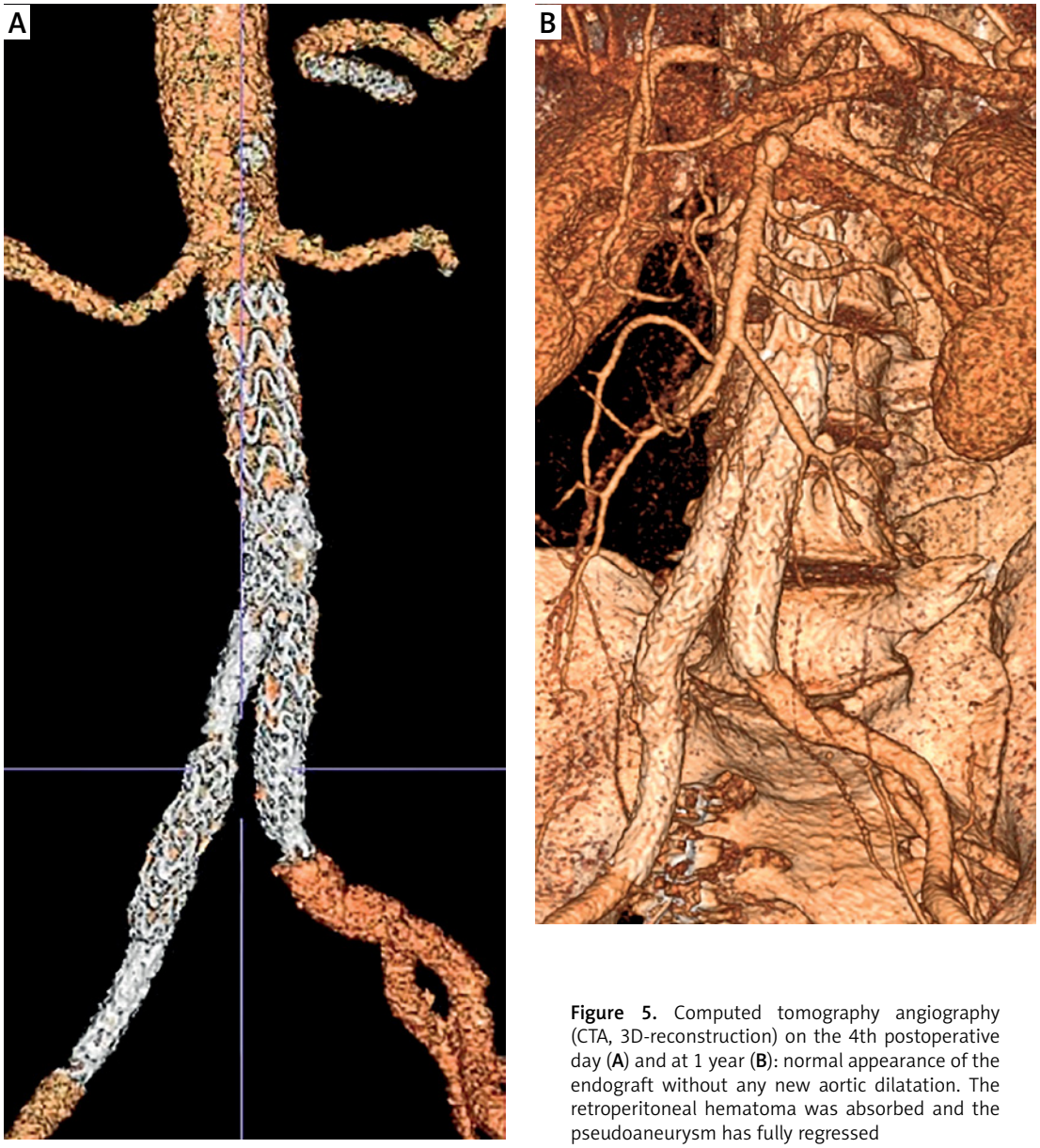

Figure 5. Computed tomography angiography (CTA, 3D-reconstruction) on the 4th postoperative day (**A**) and at 1 year (**B**): normal appearance of the endograft without any new aortic dilatation. The retroperitoneal hematoma was absorbed and the pseudoaneurysm has fully regressed

production of neurofibromin. This leads to alterations in connective and nerve tissue structure with various resulting phenotypes [3, 6, 7]. Clinical signs of NF1 may include café au lait macules, neurofibromas, axillary and inguinal freckling, Lisch nodules (iris hamartomas), skeletal abnormalities in 30–50% (kyphoscoliosis, sphenoid dysplasia or thinning of the long bone cortex, bone cysts, erosions of the bone surface), brain tumors and learning disabilities) [3, 8, 9]. Multiple lobulated neural tumors develop at the nerve trunks in the skin and the internal organs, and their locally destructive effects can be life-threatening [10, 11]. Neurofibromas are classified as localized (nodular type), diffuse or plexiform and can present as cutaneous, intraneural, or deep soft tissue lesions [10]. Cutaneous neurofibromas are benign tumors without potential for malignant transformation. Multiple paraspinal neurofibromas may arise from the spinal nerve roots [3, 10, 11]. Unlike peripherally located neurofibromas the paraspinal tumors more frequently undergo transformation into malignant peripheral nerve sheath tumors (MPNSTs) [10, 12]. Plexiform neurofibromas may cause extensive infiltration into surrounding tissues and may transform into MPNSTs in 8% to 16%. Compression of the gastro-intestinal, urinary, or pulmonary tracts by visceral neurofibromas may generate serious complications [3, 11, 13]. NF1 patients have a 34-fold increased risk for developing malignancies, including breast cancer [13, 14].

Clinical presentation of NF1 vasculopathy

Mutations in the NF1 gene result in loss of neurofibromin function, leading to dysregulated Ras/MAPK signaling. This contributes to endothelial

dysfunction, vascular smooth muscle instability, and ultimately arterial fragility, increasing the risk of aneurysm formation and spontaneous rupture. NF1 vasculopathy includes arterial stenoses, aneurysms, dissections, arteriovenous malformations, intra-neurofibromatous hemorrhage and spontaneous arterial rupture, presenting in 0.4% to 6.4% [3, 10]. On the contrary, vascular lesions are extremely uncommon in neurofibromatosis type 2 (NF 2), which is characterized by the occurrence of acoustic schwannomas, meningiomas and gliomas, among other lesions [1]. Vascular lesions develop either by proliferation of nerves within the vessel walls (spindle cell proliferation) or from pressure necrosis of the arterial wall by external compression and/or invasion by nerve sheath tumors [3, 4, 15]. Consequently, vessels become fragile and vulnerable as in other connective tissue disorders, like Marfan's and Ehlers Danlos syndrome, where the pathologic structure of the extracellular matrix may cause multiple aortic aneurysms, aortic dissection or rupture [16, 17]. NF1 lesions may appear in any artery of the body, but they have a predisposition for medium and large arteries. Consequently, they are seen more often in the renal, mesenteric, carotid, vertebral, intracranial, subclavian, innominate, coronary, peripheral arteries and the aorta [13, 14].

NF1 vasculopathy is usually asymptomatic, even in affliction of multiple vessels [8, 11]. There is a potential underappreciation of its occurrence because of the silent nature and the poor accessibility of most vascular lesions to the clinical examination. Indeed, according to an autopsy series of NF1 patients dying of other causes, vascular abnormalities were reported in 44% of them [8]. An English literature review from 1957 to 2005, reported 237 patients with NF1 [5]. Renal artery lesions with resulting renovascular hypertension were the most common finding (41%) [5, 8]. The carotid, vertebral and cerebral artery lesions were observed in 19% of patients, affecting mostly women (72%). The mean age was 38 years, varying between 22 and 54 years [10]. Veins may be also affected and spontaneous bleeding from internal jugular vein (IJV) has been reported [18, 19]. Additionally, pressure necrosis of the inferior vena cava (IVC) by a retroperitoneal neurofibroma leading to fatal retroperitoneal hemorrhage has been reported [20]. On the other hand, obstruction of the IVC by neurofibromas with a successful open repair is recorded in the literature [21]. The presence of pheochromocytomas can increase the risk of vascular rupture due to catecholamine-induced hypertension [22]. Cardiac involvement has been encountered in up to 27% of patients with NF1 with half of them having pulmonary artery stenosis [1].

Abdominal aortic coarctation or aneurysms, with or without renal and mesenteric involvement, are present in about 12% [5]. Spontaneous hemothoraces, retroperitoneal hematomas, subcutaneous and cerebral hematomas have been reported [6, 10]. Abdominal aorta involvement may be in the form of coarctation, aneurysm, acute dissection or rupture [23]. Coarctation is defined as a localized narrowing of the aortic lumen, most commonly near the ductus arteriosus. The middle aortic syndrome (MAS) is characterized by progressive narrowing of the abdominal aorta, associated with arterial hypertension and renal failure in children and young adults. It is typically compensated by the development of collateral circulation [24]. Aortic bleeding may be spontaneous, traumatic, or iatrogenic [25].

Review of the literature regarding NF 1 aortic and iliac vasculopathy

We performed a literature review regarding the affliction of the thoracic, abdominal aorta and iliac arteries in NF1 patients using the PubMed database. We found 66 patients in total, with involvement of the thoracic aorta in 23 patients, abdominal aortic involvement in 39 patients, and isolated iliac artery involvement in 4 patients. Abdominal aortic involvement was in the form of coarctation (25 patients), aneurysmal disease (8 patients) and spontaneous rupture (6 patients). Furthermore, we found 4 published cases with retroperitoneal bleeding and fatal outcome where the diagnosis of arterial erosion from neurofibromas was set postmortem [10, 26–28]. We also found 3 other published cases where no source of bleeding could be found in laparotomy [20, 25, 29]. Detailed findings of our review in each vascular segment are the following:

Thoracic aorta

Thoracic aortic involvement included 23 patients (Table I). Thirteen of them had coarctation [5, 30–38]. In 8 cases abdominal aortic coarctation was also present, and there were multiple concomitant stenoses of visceral arteries (3 affecting the celiac axis (CA), 2 the superior mesenteric artery (SMA) and 3 affecting at least one renal artery (RA), one of which had a concomitant RA aneurysm) [5, 21, 30, 32, 35, 36]. Ten of the thirteen patients were female (aged between 10 and 20 years). Nine patients were managed with open surgical repair and all survived. One patient died before receiving treatment. Two patients underwent ET, one of which had reintervention for restenosis 15 months later [21, 38].

Four patients were found with aneurysms involving the ascending aorta, aortic arch and the

Table I. Reported cases of thoracic aorta involvement in patients with NF1 vasculopathy

No.	Date of publication	Author	Pt age /sex	Type of vascular lesion	Method of repair	Outcome
Thoracic aorta coarctation						
1	May 1952	Glenn *et al.*	19/F	Coarctation of the lower thoracic and abdominal aorta proximal to the CA	Open repair using the splenic artery as bypass conduit	Patient died 1 year after the operation due to cardiac arrest after surgery for a facial neurofibroma
2	Nov 1974	Itzchak *et al.*	1/F	Tubular coarctation of the upper thoracic aorta and stenoses in major arteries and veins, including the EIAs, CA, SMA, and both RAs	Surgery was considered	Patient succumbed before management
3	Jan 1975	Rowen *et al.*	17/F	Thoracic and abdominal aortic coarctations, severe stenoses of major visceral arteries, PDA, stenosis of the SMA, possible right RA stenosis, duplicated left RAs	1) Open surgical aorto-aortic graft from the distal thoracic aorta to the infrarenal aorta 2) Open surgical correction of thoracic coarctation with an end-to-side anastomosis of the distal aorta to the left subclavian artery and PDA closure	Uneventful recovery
4	Sep 1974	Neiman *et al.*	4/F	Aortic coarctation distal to the origin of the left SA	[No information]	
5	Apr 1985	Donaldson *et al.*	14/M	3 cm coarctation of the thoracic aorta	Open surgical excision of the coarctated segment and aortic repair with woven dacron graft	Uncomplicated recovery. BP controlled without antihypertensive agents at year 1 post-operatively
6	1997	Mickley *et al.*	18/F	Atypical aortic coarctation	Thoraco-abdominal aorto-aortic bypass	Patient recovery, BP controlled without antihypertensive agents over a 9-year follow-up period
7			27/F	Atypical aortic coarctation	Thoraco-abdominal aorto-aortic bypass	Patient recovery, BP controlled without antihypertensive agents over a 9-year follow-up period
8			13/M	Atypical aortic coarctation	Thoraco-abdominal aorto-aortic bypass	Patient recovery, BP controlled without antihypertensive agents over a 9-year follow-up period
9	Jun 2002	Connolly *et al.*	17/M	Coarctation of the distal descending aorta extending to the pararenal abdominal aorta, saccular left RA aneurysm	Open aortic bypass (dacron graft), aortorenal bypass	Patient recovery, BP controlled over an 8-year follow-up period

Table I. Cont.

No.	Date of publication	Author	Pt age /sex	Type of vascular lesion	Method of repair	Outcome
10	Sep 2007	Oderich *et al.*	22/F	Thoracoabdominal aortic aneurysm, coarctation, supraceliac aortic aneurysm, occluded CA	Descending thoracis to pararenal aortic bypass, aorto-SMA bypass	Patient recovery, control of BP, over a 4-year follow-up period
11	Mar 2013	Kimura *et al.*	4/F	5 cm hourglass-shaped coarctation of the thoracic aorta	Open surgical excision of the coarctated segment and aortic repair with ePTFE graft	Uncomplicated recovery. BP controlled under ACE inhibitor
12	Aug2014	Mavani *et al.*	32/F G1P0	Coarctation of the thoracic aorta	Endovascular stenting	Patient recovery, BP controlled under one anti-hypertensive agent
13	Feb 2015	Omeje *et al.*	7/F	Coarctation of the proximal descending thoracic aorta with a hypoplastic abdominal aorta and cor triatriatum dextrum	Endovascular stenting of the coarctated segment	Initial success, re-intervention 15 months later to dilate the stent. Patient underwent surgical correction via resection of the fibromuscular tissue obstructing the inferior vena cava. Patient recovery, no recurrence over a 2-year follow-up period
Ascending aorta and proximal descending thoracic aorta aneurysm						
1	May 1981	Pentecost *et al.*	7/F	1) Left VA aneurysm at 16 months of age 2) Proximal ruptured descending aortic aneurysm involving the left SA and VAs	Open surgical exploration of the thorax via thoracotomy. Resection of the aortic aneurysm and graft reconstruction	Patient sustained hypoxic cerebral damage due to significant bleeding during graft placement
2	Sep 2007	Oderich *et al.*	20/F	Ascending aortic aneurysm	Conservative treatment	Asymptomatic over a 4.3-year period
3			68/M	Ascending aortic aneurysm, AAA and bilateral CIA aneurysms	Aortoiliac bypass	Patient died due to unknown cause 4 months after operation
4	Jul 2012	Hirooka *et al.*	57/M	Ascending aortic aneurysm	Open resection of the aneurysm	
Thoracoabdominal aneurysms						
1	Sep 2007	Oderich *et al.*	43/F	Prior ruptured thoracoabdominal aortic aneurysm, left SA aneurysm (5 cm) and VA aneurysm	Left SA ligation, carotid-subclavian artery bypass	Patient recovery, asymptomatic over a 7.5-year follow-up period
2			75/M	Ascending aortic and thoracoabdominal aneurysms	Conservative treatment	Patient death of unrelated cause
3			72/F	Ascending aortic and descending thoracoabdominal aneurysm	Aortoaortic graft	Patient death due to ruptured ascending aortic aneurysm, 2.6 years post-operation

Table I. Cont.

No.	Date of publication	Author	Pt age /sex	Type of vascular lesion	Method of repair	Outcome
Intramural hematoma						
1	Mar 2002	Ali *et al.*	45/F	Intramural hematoma of the distal aortic arch and proximal descending aorta	Conservative treatment (HR and BP control in an ICU setting)	Complete resolution 1 month later, no underlying pathology at 3 months
Spontaneous rupture						
1	Sep 2016	Kotopoulos *et al.*	46/F	Traumatic rupture of the thoracic aorta		Patient death before management, post-mortem diagnosis
2	Nov 2019	Tateishi *et al.*	42/F	Spontaneous ascending aorta rupture (8 mm tear) during pregnancy	Open excision and ascending aorta replacement, cesarean section and hysterectomy (emergent)	7-year follow-up period without major changes

Pt – patient, M – male, F – female, CA – celiac artery, EIA – external iliac artery, SMA – superior mesenteric artery, CIA – common iliac artery, RA – renal artery, PDA – patent ductus arteriosus, SA – subclavian artery, BP – blood pressure, ePTFE – expanded polytetrafluoroethylene, AAA – abdominal aortic aneurysm, VA – vertebral artery, HR – heart rate, ICU – intensive care unit.

proximal descending aorta [5, 39, 40]. In one ruptured aneurysm, significant intraoperative bleeding led to the patient's death [39]. One of these patients also had an abdominal aortic aneurysm and bilateral common iliac artery aneurysms and good outcome after abdominal aortic open reconstruction [5]. The third patient was treated conservatively and was alive after 4 years and the fourth patient had a successful open repair [40]. Three patients had thoracoabdominal aneurysms. One of them was treated conservatively and the other two underwent open repair; the first later developed a new subclavian and vertebral artery aneurysm and the second died 2.6 years postoperatively of a ruptured recurrent ascending aortic aneurysm developed at the previous operating site [5]. There was 1 patient with aortic arch intramural hematoma who was treated conservatively with a successful outcome, and 2 patients with a spontaneous rupture of the aorta, one of which died before receiving treatment [41–43]. The other was a pregnant woman who was in good condition 7 years after open repair [43].

Abdominal aorta

Abdominal aortic coarctation

Isolated abdominal aortic coarctation (not involving the thoracic aorta) occurred in 25 patients (Table II) [5, 44–62]. Seven of them were treated conservatively (one of them was treated surgically for a cerebellar tumor which resolved her symptoms), 14 with open aortoplasty and/or bypass to renal and/or to mesenteric arteries (one of which was managed with supplementary stenting due to recurrence of hypertension and compression of the graft by enlarging neurofibromas). Four patients were treated with balloon renal angioplasty. One of them underwent angioplasty of the coarctated aortic segment, while 2 of them had no intervention in their mild aortic narrowing. Interestingly, one of these patients with recoarctation after initial surgical treatment exhibited dissection after stent re-dilation, which was managed with placement of numerous overlapping stents [58]. There was no mortality in all cases. In all cases blood pressure was corrected except 1 case with splenorenal bypass [44]. Re-intervention was required in 3 patients [55, 58, 62].

In 23 patients there were concomitant abnormalities in renal arteries (stenoses in 21 patients, bilateral in 14, narrowing and irregular course in 1 patient [45] and aneurysm in 1 patient [5]). Celiac axis was affected in 4 patients, SMA stenosis was present in 7 patients (one developed a post-stenotic aneurysm), detached SMA in 1 patient with retrograde flow from collateral networks [47], IMA stenosis was present in 3 patients, one after surgical correction [58] and functionally occluded in the second patient. Iliac arteries were involved in 2 patients (tortuosity in 1 patient) [45].

Spontaneous abdominal aortic rupture

Spontaneous abdominal aortic rupture was detected in 6 patients (Table III) [6, 12, 15, 23, 63, 64]. The first case of massive retroperitoneal hemorrhage due to rupture of a fragile abdominal aorta in an NF1 patient was reported by Wiger *et al.* in 1997 in a 35-year-old female [15]. Avulsion of the left 4th lumbar artery occurred due to a ruptured lumbar artery aneurysm. Aortic fragility

Table II. Reported cases of isolated abdominal aortic coarctation in patients with NF 1 vasculopathy

No.	Date of publication	Author	Pt age	Type of vascular lesion	Method of repair	Outcome
1.	Sept 1963	Bloor *et al.*	21/F	Coarctation of the abdominal aorta presenting with gestational hypertensive spike, abnormal right RA origin	Open exploration of the abdomen, anatomy not well recognizable. Splenectomy due to splenomegaly. Spleno-renal bypass	Operation did not help improve patient's hypertension
2.	Jun 1971	Aquino *et al.*	28/M	9 cm long infrarenal aortic stenosis, tortuous iliac arteries, with post-stenotic dilatation, narrowed and irregular proximal left RA	Conservative treatment	Patient with uncontrolled BP under antihypertensive treatment
3.	May 1973	Mena *et al.*	13/M	Long narrowing of the lower abdominal aorta and stenosis at the origin of the left RA	Open left aorto-renal venous graft	Patient recovery, BP controlled postoperatively
4.			16/F	Infrarenal abdominal aortic coarctation	Conservative treatment was decided due to severe CNS involvement	
5.	Nov 1975	Schürch *et al.*	10/F	Coarctation of the abdominal aorta and bilateral RA stenoses	Open surgical resection of stenotic intervals and reimplantation of renal arteries on coarctated aorta	Uneventful recovery, hypertension due to RA restenosis, progression of the coarctation, IMA restenosis, anti-hypertensive medications over a 5-year follow-up period
6.	Mar 1977	Rosenbusch *et al.*	26/F	Abdominal aortic coarctation with detached SMA, rich collateral networks	Conventional treatment	High BP under antihypertensive treatment
7.	Nov 1982	Guthrie *et al.*	14/F	Abdominal aortic coarctation and bilateral RA stenoses, SMA stenosis	[removal of cerebellar tumor]	Remission of hypertension without intervention regarding the coarctation
8.	Jan 1984	Zochodne	16/F	Abdominal aortic coarctation and stenoses of multiple visceral arteries (RAs, SMA, CA)	Conservative treatment	
9.	Jul 1985	Tenschert *et al.*	35/M	Coarctation of the abdominal aorta and bilateral RA stenosis	Conservative treatment	BP controlled with anti-hypertensive agents
10.	May 1986	MSGH	18/M	Abdominal aortoiliac coarctation with stenosis of the left RA, CA, SMA, IMA	Open repair of coarctation and visceral artery stenoses with a dacron bypass graft from the distal thoracic aorta to the proximal iliac arteries	Uneventful recovery, BP controlled under antihypertensive agents, 5 months postoperatively
11.	Jan 1990	Mengden *et al.*	42/M	Coarctation of the abdominal aorta and bilateral RA stenosis	Conservative treatment	Patient alive and well over a 13-year follow-up period

Table II. Cont.

No.	Date of publication	Author	Pt age	Type of vascular lesion	Method of repair	Outcome
12.	Jan 1991	Zwaan *et al.*	38/F	Infrarenal aortic coarctation and restenosis of the right RA with post-stenotic dilatation (percutaneous angioplasty one year before)	Open surgical patch angioplasty to the stenotic aorta and re-stenotic RA	(-)
13.	1995	Ing *et al.*	17/M	Supra- and pararenal abdominal aortic coarctation with stenoses of multiple visceral arteries = bilateral RA stenoses, CA, SMA	1) Open surgical repair with trifurcated graft from the proximal abdominal aorta to the SMA including the two RAs. 2) Further management with endovascular stent placement in the abdominal aorta and RAs bilaterally due to recurrence of hypertension and compression of the graft by neurofibromas	Patient recovery, BP controlled under several antihypertensive agents over a 6-month follow-up period. Re-stenting of the left renal artery at month 7 post-intervention
14.	Jan 1995	De Gregorio *et al.*	6/M	Aortic coarctation and bilateral RA stenosis	Balloon angioplasty of both RAs and aortic lesions	Recovery, normal renal function at year 1 post-intervention, normal BP, no recurrent stenoses
15.	May 1997	Kurien *et al.*	4/F	Abdominal aortic coarctation and eventually bilateral RA stenosis	Ballon aortoplasty	Restenosis
16.	Aug 2000	Khan, Moore	15/F	Abdominal aortic coarctation, bilateral RA stenosis and SMA stenosis after attempted surgical correction, right nephrectomy and autotransplantation of the left kidney, presented with recoarctation and aortic dissection after stent redilation	1) Surgical correction, right nephrectomy and autotransplantation of the left kidney 2) Attempt to control contrast extravasation with overlapping stents due to recurrence of extravasation with each new stent. 2 days after the first intervention, a pseudoaneurysm had organized, actively filling, managed with overlapping stents with an additional ultra-thin Gore-Tex pericardial membrane covering	Eventual uneventful recovery and symptom resolution, no recurrence over a 2-month follow-up period

Table II. Cont.

No.	Date of publication	Author	Pt age	Type of vascular lesion	Method of repair	Outcome
17.	May 2002	Criado *et al.*	11/F	Mid-abdominal aortic coarctation affecting the origin of the CA, SMA and right RA, and a left RA stenosis	Open repair (retroperitoneal approach) utilizing the left hypogastric artery and a PTFE patch	Patient recovery with minimal residual aortic stenosis due to patch width, BP normotensive without antihypertensive agents over a 22-month post-operative follow-up period
18.	Sep 2007	Oderich *et al.*	6/F	Abdominal aortic coarctation with bilateral RA stenoses	Open abdominal aortoplasty and bilateral RA bypass	Patient recovery, well controlled BP, over a 3-year follow-up period
19.			9/M	Abdominal aortic coarctation with right RA and SMA stenoses	Open supra-celiac to infra-renal artery bypass, aorto-renal artery and aorto-SMA bypass	Patient recovery, control of BP, over an 8-month follow-up period
20.			17/M	Abdominal aortic coarctation, bilateral RA stenoses and left RA aneurysm	Open abdominal aortoplasty, bilateral RA bypass	Patient recovery, control of BP, over a 11.5-year follow-up period
21.	2008	Pardo *et al.*	16/F	Abdominal aortic coarctation and right RA stenosis + functional occlusion of the SMA	Open aorto-aortic bypass and right RA reimplantation	Patient normotensive 4 years post-operation
22.	Apr 2017	Veean *et al.*	Adolescent	Abdominal aortic coarctation and atrophic left kidney	Open bypass graft	
23.	Feb 2020	Raborn *et al.*	8/F	MAS with mild narrowing of the infrarenal aorta and bilateral ostial RA stenoses	Percutaneous transluminal balloon angioplasty of the left and right RAs	Patient with well-controlled hypertension under 1 antihypertensive agent for 8 years post-intervention and repeat angioplasty of the left renal artery due to restenosis
24.			4/F	MAS with narrowing of the infrarenal aorta with bilateral ostial RA stenoses	Percutaneous transluminal balloon angioplasty of the left and right RAs	Patient with well-controlled hypertension under 1 antihypertensive agent at 6 months post-intervention
25.	Sep 2020	Azadi *et al.*	49/F	L1 to L4 stenosis of the suprarenal to infrarenal abdominal aorta, bilateral RA stenoses and IMA stenosis	Open aneurysm repair with renal and inferior mesenteric artery bypass	Follow-up CT with patent bypass grafts

Pt – patient, M – male, F – female, RA – renal artery, BP – blood pressure, CNS – central nervous system, IMA – inferior mesenteric artery, SMA – superior mesenteric artery, CA – celiac artery, PTFE – polytetrafluoroethylene, MAS – midaortic syndrome, L1-4 – lumbar vertebra 1 to 4, CT – computed tomography.

Table III. Reported cases of spontaneous abdominal aortic rupture in patients with NF1 vasculopathy

No.	Date of publication	Author	Pt age/ sex	Ruptured vessel	Method of repair	Outcome
1	Mar 1997	Wigger *et al.*	35/F	1.5 cm aneurysm of the left 4th lumbar artery leading to avulsion	Open laparotomy, repair by 14 mm PTFE graft interposition	Uneventful recovery, no recurrence at 24- month follow-up
2	Aug 2001	Chew *et al.*	34/M	3 cm aortic tear above the bifurcation, aortic dissection, small aneurysm of the left CIA	Open laparotomy, primary suturing	Uneventful recovery
3	Nov 2002	Hines *et al.*	52/M	Infrarenal aorta	Open laparotomy, neurofibroma resection, failed attempts of primary repair and patch angioplasty	Patient death
4	Apr 2008	Hinsch *et al.*	28/F	Active retroperitoneal bleeding possibly from the lumbar artery	Open laparotomy, failed attempts to recognize the culprit vessel, manipulations led to further vessel injury, failed attempts for primary repair	Intraoperative patient death
5	Jan 2010	Falcone *et al.*	49/F	Infrarenal aorta	Endovascular grafts	Patient death at the 15th post-operative day
6	Jan 2022	Wang *et al.*	41/F	5 cm tear at aortic bifurcation	Caesarean section before open laparotomy	Intraoperative patient death
	Present case		55/M	Spontaneous infrarenal aortic rupture due to avulsion of the IMA	EVAR – coil embolization of the right IIA	Uneventful recovery, no recurrence at 1-year follow-up

Pt – patient, M – male, F – female, PTFE – polytetrafluoroethylene, CIA – common iliac artery, IMA – inferior mesenteric artery, EVAR – endovascular abdominal aortic repair, IIA – internal iliac artery.

prevented direct suturing during open repair and a 14 mm PTFE graft was successfully interposed. At 24 months' follow-up no complications were detected. The second case was reported by Chew *et al.* in 2001 in a 34-year-old male [23]. A 3 cm long aortic tear above the aortic bifurcation along with aortic dissection was managed successfully with primary suturing. A left common iliac artery aneurysm was apparent. This is the only case where acute abdominal aortic dissection was reported. The third was reported by Hines *et al.* in 2002 in a 52-year-old male [63]. An aortic rupture below the renal arteries from an adjacent neurofibroma's invasion resulted to death after failed attempts for patch angioplasty. The neurofibroma was resected but the patient died from disseminated intravascular coagulation. The fourth case was reported by Hinsch *et al.* in 2008 in a 28-year-old female [12]. Vascular fragility led to the patient's death after failed attempts to repair hemorrhage from a lumbar artery as surgical manipulations resulted in further vessel injury. The fifth case was reported by Falcone *et al.* in 2010 in a 49-year-old female [6]. A 2.5 cm infrarenal tear from a spindle cell neurofibroma was technically successfully treated with aortic cuffs but the patient died at the 15th p.d. from anoxic brain injury. The sixth case was reported by Wang *et al.* in 2022 in a 41-year-old pregnant woman undergoing labor, who died due to a 5 cm tear of the abdominal aortic bifurcation which deemed irreparable intraoperatively [64]. Therefore, 7 patients were treated for spontaneous abdominal aortic rupture, 5 with OR and 2 with EVAR (including our case). Three of the 5 patients died after OR, 2 intraoperatively while 1 of the 2 patients died after EVAR.

Abdominal aortic aneurysms

Abdominal aortic aneurysms (AAA) were detected in 8 patients (Table IV) [5, 8, 14, 16, 65]. The first case of an intact AAA was reported by Oderich *et al.* in 2007 in a 77-year-old male [5]. OR with graft interposition was effective and a 5-year follow-up was normal. The same authors reported a second patient (74-year-old male) who died during OR repair due to a ruptured AAA. He had concomitant bilateral internal carotid and vertebral artery aneurysms. They additionally reported a third patient (68-year-old male) with concomitant thoracic and bilateral common iliac artery aneurysms, who underwent a successful aortoiliac bypass and died 4 months after the operation from unknown causes. A fourth patient (71-year-old male) reported by the same authors with aneurysmal-occlusive disease was treated

Table IV. Reported cases of isolated abdominal aortic aneurysms in patients with NF1 vasculopathy

No.	Date of publication	Author	Pt age/ sex	Type of vascular lesion	Aneurysm diameter (mm)	Rupture	Method of repair	Outcome
1	Sep 2007	Oderich *et al.*	77/M	AAA		(-)	Aortoaortic graft	Patient alive at 5-year follow-up
2			74/M	AAA		(+)	Left thoracotomy	Patient died intraoperatively
			68/M	Ascending aortic aneurysm, AAA and bilateral CIA aneurysms		(-)	Aortoiliac bypass	Patient died due to unknown cause 4 months after operation
3			71/M	AAA with aortoiliac occlusive disease			Aortobifemoral bypass	Patient recovery with no recurrence at 6-year follow-up
4	Apr 2012	Park *et al.*	49/M	Infrarenal AAA aneurysm	1) 3 × 3.5 cm, saccular 2) 2 × 3 cm	(+)	1) EVAR (another institution) 2) Open surgical repair of recurrent aneurysm, EVAR grafts removal and reconstruction 3) Post-operative middle colic artery branch coil embolization	Patient recovery
5	May 2012	Hori *et al.*	78/M	Infrarenal AAA	55 mm	1) (-) 2) (+)	1) EVAR 2) Open laparotomy, which revealed penetration of the graft through the aortic wall. Graft and aneurysm excision	Regression of lymphadenopathy
6	Jan 2019	Moro e*t al.*	67/F	Infrarenal AAA, aortocaval fistula	34 mm	(+)	1) EVAR 2) Redo-EVAR (Ib endoleak) 3) Left IIA aneurysm coil embolization 4) Left hemicolectomy and colostomy creation due to rupture of 2 new left colic artery aneurysms	Patient recovery
7	Feb 2022	Nakai *et al.*	78	AAA	45 mm	(+)	EVAR	Patient recovery

Pt – patient, M – male, F – female, AAA – abdominal aortic aneurysm, CIA – common iliac artery, EVAR – endovascular abdominal aortic aneurysm repair, IIA – internal iliac artery.

successfully with aorto-bifemoral bypass, having a normal 6-year follow-up. The fifth case was reported by Park *et al.* in 2012 in a 49-year-old male [8]. OR was successful after EVAR performed in another institute for a ruptured aortic pseudoaneurysm. The indication for OR was a new pseudoaneurysm at the aortic bifurcation. On the 6th p.d. coil embolization was performed for a bleeding middle colic artery branch with good outcome. The sixth case was reported by Hori *et al.* in 2012 in a 78-year-old -male [16]. He was initially treated with EVAR for an intact aneurysm but 3 months later with OR for rupture. Perigraft lymphadenopathy and fibrotic granulomas were observed. The seventh case was reported by Morro *et al.* in 2019 in a 67-year-old female with a ruptured AAA (sized 3.4 cm) and concomitant aortocaval fistula who underwent EVAR and redo-EVAR on the 4th p.d. due to Ib endoleak (a coil embolization of a left IIA aneurysm was also performed) [14]. Emergency left hemicolectomy and transverse colon colostomy were performed due to rupture of 2 new left colic artery aneurysms on the 22nd p.d. with good outcome. The eighth case was reported by Nakai *et al.* in 2022 in a 78-year-old female [65]. She underwent a successful EVAR for a ruptured AAA (4.5 cm in diameter). A small asymptomatic pseudoaneurysm was developed at the proximal landing zone on the 7th p.d. and tracheostomy was needed due to a spontaneous cervical hematoma which later was related to a new left vertebral pseudoaneurysm. The patient survived.

Therefore, 5 patients were treated for intact AAAs, 3 with OR and 2 with EVAR. All patients survived the first 30 days (1 died after 4 months from unknown causes). Three patients were treated for ruptured AAAs, 1 with OR who died intraoperatively and 2 with EVAR who survived. Thirty-day mortality was 0 in intact AAAs, 33% in ruptured AAAs and 57% in spontaneous aortic ruptures. Total 30-day mortality in ruptured cases (AAAs and spontaneous abdominal aortic ruptures) was 50% (5 out of 10) resembling the mortality of ruptured aneurysms in the general population. In detail, 30-day mortality was 66% in ruptured cases after OR and 25% in ruptured cases after EVAR. This superiority of EVAR in 30-day mortality may make its use more widespread in the future.

Iliac arteries

Iliac arteries were affected in combination with aortic involvement in 2 patients [5, 23]. Isolated iliac involvement has been reported in 4 patients (Table V) [5, 7, 66, 67]. The first patient with a 6-cm CIA tear died before receiving treatment [66]. The

Table V. Reported cases of isolated common, internal and external iliac artery aneurysms in patients with NF1 vasculopathy

No.	Date of publication	Author	Pt age/ sex	Affected vessel	Aneurysm diameter [mm]	Rupture	Method of repair	Outcome
1	Nov 1997	Kunz *et al.*	36/M	6 cm left CIA tear		(+)		Patient death
2	Dec 2021	Kamada *et al.*	40/F	1) Ruptured left IIA aneurysm, AVF 2) Newly developed aneurysm	2) 50 mm, increase to 55 mm within 3 days	(+)	1) Open repair, femorofemoral bypass 2) Failed conservative management 3) Coil embolization under ultrasound-guided direct percutaneous puncture	Patient recovery
3	Sep 2007	Oderich *et al.*	72/M	Right CIA aneurysm		(-)	Conservative treatment	Patient recovery no recurrence at 4.5-year follow-up
4	June 2023	Uzuka *et al.*	49/M	Fusiform aneurysm of the right EIA-CFA	50 mm	(-)	1) Open repair with graft placement 2) Re-operation for 26-mm right deep femoral artery aneurysm	Patient recovery. Re-operation at the 6th post-operative year. No recurrence since then at 9-year follow-up

Pt – patient, M – male, F – female, CIA – common iliac artery, IIA – internal iliac artery AVF – arteriovenous fistula, EIA – external iliac artery, CFA – common femoral artery.

second patient with a ruptured left IIA aneurysm and an AVF was treated surgically with a femoro-femoral bypass. A newly developed aneurysm at the same site post-operatively was treated with ultrasound-guided coil embolization with good results [67]. The third patient with a right CIA aneurysm was treated conservatively with satisfactory mid-term follow-up [5]. The fourth patient with an EIA-CFA aneurysm was treated surgically. Six years later a re-do operation was performed for a profunda aneurysm with good outcome [7]. Consequently, OR repair had satisfactory results in iliac aneurysms.

Screening for NF1 vasculopathy

It is reported that vascular lesions are present in every NF1 patient if careful examination is performed and no vessel including veins is excluded [68, 69]. Some investigators suggest screening of all patients with non-invasive imaging modalities (color duplex, magnetic resonance angiography, and computed tomography scanning) [23]. Imaging must include the head, chest, and abdomen [64]. The need to assess systemically great vessels in patients with NF1 is emphasized [64]. On the other hand, other reports claim that regular vascular assessment is not recommended to all NF1 patients, as clinically significant lesions are relatively uncommon (2%). They advocate selective imaging when symptoms or clinical suspicion are apparent [5]. It is reasonable that NF1 patients should be systematically screened for vascular lesions from the third decade of life to prevent fatal complications secondary to the aneurysm rupture [70]. The mean screening interval has not been clarified but a yearly color duplex for the accessible arteries would be sensible though a whole-body CTA or MRA should be based on the physician's judgement.

Pathology and pathophysiology of NF1 vasculopathy

The vascular fragility in NF1 is attributed to multiple mechanisms, including elastin degradation, defective smooth muscle cell function, and ischemia of the vasa vasorum, leading to medial necrosis. These changes predispose affected arteries to spontaneous dissection, aneurysm formation, and, in rare cases, complete arterial avulsion. Additionally, external compression by adjacent neurofibromas may exacerbate vessel wall instability, further increasing the risk of rupture. Arteries of any size can be afflicted in NF1. The lesions in arteries smaller than 1 mm in diameter were described by Reubi as pure intimal, intimal aneurysmal, and nodular, alone or in various combinations [28]. The proliferation of intimal spindle cells obliterates the vascular lumen. In ruptured aortas, the aortic wall is described to demonstrate medial elastolysis, mucoid degeneration, increased numbers of adventitial S 100-positive cells in one report [15] and medial thinning and degeneration of the elastic lamina, adventitial fibrosis and foreign-body granulomas in another report [8]. The observed elastolysis and medial thinning have been reported as the most likely responsible mechanisms for aneurysmal dilatation and dissection [10]. Several reports note friable vascular walls [23, 63]. Although histological evaluation is missing in several cases, the elastolysis and medial thinning described above are likely causes of arterial wall friability. Loss of neurofibromin expression in endothelial cells has been implicated in abnormal vascular smooth muscle proliferation and structural arterial fragility [10].

Extravascular pressure from neurofibromas can additionally result in luminal stenosis in larger size arteries [13], while infiltration of the wall of a large artery by a neurofibroma or ganglioneuroma has been reported to be associated with massive hemorrhage resulting in the patient's death [10]. Cury *et al.* proposed two hypotheses for the causes of arterial rupture: 1) weakening of the vessel wall due to neurofibromatous invasion of the tunica media; 2) compression of the vasa vasorum of the large artery by neurofibromatous tissue, resulting in weakening of the arterial wall. Aortic disease due to adventitial compression from proliferation of Schwann cells followed by secondary changes of fibrosis presents as stenotic or occlusive disease. Alternatively, direct invasion by Schwann cells with intimal thickening and destruction of the media and elastic tissue leading to aneurysm formation may also be present [71].

Indications for treatment

As evidence is limited, no specific treatment strategies or precise indications for intervention are recommended [13]. Regarding aortic aneurysms, the actual size criteria for intervention are unknown because of the rarity of this disease. Clinical judgment is required, and treatment should be individualized [23]. Some claim that only symptomatic cases must be treated while others suggest that indications should be the same as for patients without NF1 [6]. Prophylactic percutaneous endograft relining of the infrarenal aorta to prevent aortic invasion in patients with known retroperitoneal invasion has also been suggested. The long-term effects of this approach are unknown [6]. Additionally, as plexiform neurofibromas are extremely vascular and may contain ecstatic vessels or aneurysms, preoperative embolization can minimize possible bleeding complications [10]. The European Society for Vascular Surgery 2024 Clinical Practice Guidelines recommend

that the threshold diameter for considering repair in patients with AAAs and an underlying genetic cause should be individualized, depending on the underlying genetics and anatomy [26]. Of course, saccular aneurysms warrant repair regardless of their size. It is notable that the diameter of the ruptured AAAs in our review was below 5 cm in the 2 cases where the size is reported [14, 65]. This raises concerns for a decrease to the diameter threshold especially when aneurysm configuration is not thoroughly fusiform.

Treatment

The fragility of the arterial wall influences not only the potential aneurysm formation or rupture but also the type and efficacy of treatment. Open reconstruction may be successful but has been invariably associated with disastrous results as arterial clamping and suturing cause further arterial wall damage [23]. Severe perioperative complications have been reported so far, like intra- or postoperative uncontrolled bleeding. In one report of infrarenal aortic rupture, the aorta was so friable that even pledgeted sutures tore through the aortic wall and the patient eventually died [63]. In another report, a spontaneous hemorrhage of the infrarenal aorta, as a left lumbar artery torn out of the aortic wall, was successfully repaired using interrupted sutures with Teflon pledgets [15]. In open reconstruction even the self-retaining retractor may cause damage to visceral blood vessels. Thus, special attention is required regarding the retraction of the bowel and its mesentery [8]. Successful outcome was reported elsewhere, where pledgeted sutures and packing achieved safe repair in a large spontaneous tear near the aortic bifurcation [23]. Extra-anatomic bypass has been suggested with infrarenal aortic ligation, but no such report exists in the literature [6]. However, a healthy infrarenal aorta is required to achieve a safe aortic stump creation. Not only vessel friability but the extreme vascularity of the potentially surrounding neurofibromatous tissue is a concern in open surgery [23]. Large neurofibromas have a gelatinous consistency and thus fragment easily after surgical manipulations. The friable vessels tear and avulse easily from each other with profuse bleeding and ligatures and electrocautery may not achieve effective hemostasis [63, 72]. In some cases, aneurysmal ligation and bypass grafting is preferable, in contrast to direct repair, to avoid the infiltrating vascular neurofibromatous tissues [23]. If open surgery is going to be used, specific repair techniques to avoid iatrogenic vessel injury are needed, like delicate and atraumatic handling of tissues, careful positioning of retractors and use of soft and protected arterial clamps. Moreover, grossly healthy-appearing aortic segments at anastomotic sites must be used. Sewing the anastomoses with pledgeted sutures, and use of supporting cuffs and glues are also needed [5, 8, 65, 73]. Overall, open surgical repair in NF1 patients presents unique challenges due to the friability of vessel walls, increased risk of anastomotic dehiscence, and potential interference from adjacent neurofibromas. While OR remains an option for anatomically unfavorable cases, endovascular repair (EVAR) offers a minimally invasive alternative with reduced perioperative morbidity in these high-risk patients.

On the other hand, endovascular repair has uncertain durability in the future due to the diffuse and progressive nature of NF1 vasculopathy [74]. It may cause intimal tears or secondary pseudoaneurysm formation due to radial and spring back forces of the stent graft against a fragile wall, which usually require additional treatment [6, 8, 14, 65, 74]. Careful manipulation of wires is also recommended as these vessels may be vulnerable to dissection [6]. The first case of ET of arterial rupture in an NF1 patient was described by Falcone *et al.* [6]. A spontaneous infrarenal aortic rupture was treated with EVAR and an intimal erosion at the inferior level of the endograft was found postmortem. A neurofibroma which had infiltrated the wall of the aorta was the culprit lesion [6]. In another case, 3 months after EVAR, periaortic lymphadenopathy caused deformation of the aneurysm, and the endograft migrated and penetrated the wall. Open repair was successful [16]. The long-term reaction of the friable aortic wall to stent-grafting and the durability of prevention on vascular wall invasion remains unknown [6]. Currently there is no consensus as to which type of treatment is better. Traditionally, the presence of a genetic or heritable aortic condition has been considered a contraindication to endovascular intervention [17]. ESVES guidelines recommend as the first option, open surgical repair for abdominal aortic aneurysms in young patients with suspected connective tissue disorders [73]. However, EVAR may be offered in the emergency setting as it is associated with decreased morbidity and mortality compared to open surgery, even if it is a bridging procedure to a more definitive repair [17]. It would also be worth considering for patients who are not candidates for open surgery, who are at high risk for reintervention, or who have a previous graft implantation or multiple redo procedures even if they have a genetic or heritable aortic condition [17]. For these reasons a gradual move towards endovascular repair has been observed [73]. However, EVAR cannot yet be recommended for routine use in patients with underlying genetic causes and predisposition to aortic fragility and continued aortic dilatation

as its durability is uncertain [73]. Nevertheless, management in patients with an underlying genetic cause should be carried out in a highly specialized center by a multidisciplinary aortic team [17]. Nowadays, it remains controversial whether endovascular or open surgery is appropriate for NF1 patients with aortic pathology AAA [8, 14, 23, 65]. While EVAR was deemed the most suitable approach in this case, open repair (OR) remains an alternative, particularly in younger patients with favorable anatomy. However, NF1-related vascular pathology presents unique challenges for OR, including increased tissue friability, a higher risk of perioperative complications, and potential difficulty in achieving durable anastomoses. In addition to EVAR, adjunctive endovascular techniques, such as coil embolization of the avulsed IMA or the use of covered stents, could also be considered depending on the extent of vessel injury and aneurysm characteristics.

As we mentioned above, postoperative complications due to arterial fragility have been reported after EVAR, like aortic wall injury, development of new (secondary) ruptured aneurysms in a splanchnic artery or unpredictable bleeding at remote sites [6, 8, 65]. Sometimes bleeding occurs in areas where previous operations have been performed. In one report, bleeding from a disrupted paraspinal artery occurred postoperatively in a remote site of a previous orthopedic procedure for scoliosis [10]. Intraluminal tumor and thrombus were found in the artery postmortem [10].

Regarding spontaneous bleeding and aneurysms of other arteries, ET with coil embolization or percutaneous stent graft placement, are often considered preferable when it is mandatory to maintain an efficient blood flow in the regions perfused by the targeted vessel. This approach is less invasive and has low intra-operative and post-operative mortality [74]. Although, there are concerns about the increased risk of complications with diagnostic angiography and other catheter-based procedures in NF1 patients, in a recent systematic review, it is concluded that ET is safe and effective even in hemodynamically unstable NF patients at all ages [74]. Notably, this review did not include aortic pathology [74]. Finally, it is worth mentioning that no case was encountered in thoracic aorta with primary aortic dissection. In one reported case, a Stanford type B aortic dissection was a complication of percutaneous intercostal aneurysm embolization with good outcome under medical treatment [75].

To sum up, previous reports have highlighted the variability in outcomes between EVAR and OR in NF1-related vascular emergencies. While OR offers definitive repair, it is associated with higher morbidity due to increased surgical complexity in these fragile vessels. EVAR, on the other hand, has demonstrated promising results in achieving immediate hemostasis with a lower perioperative risk, although concerns regarding long-term durability persist. A comparative analysis of available cases suggests that patient selection is critical, with EVAR favored in high-risk surgical candidates and anatomically feasible cases.

Survival

Patients with NF1 die at a median age of 59 years. That means that they die 15 years younger than controls matched for age and sex [76]. Overall patient survival is 77% at 10 years in contrast to 87% for the expected survival of a matched population [5]. The most common cause of death is malignancy. Vascular disorders are the second cause of death, especially among those patients aged 40 years old [5, 76, 77].

Follow-up

Lifelong surveillance is important after EVAR or TEVAR as potential continued expansion of the aneurysm and the vulnerable aorta at the native proximal and distal landing zones may occur [17, 77]. Consequently, any new intimal tears, endoleaks, dissections or endograft migration necessitate repeat interventions in up to 35% of cases [17]. Given the progressive nature of NF1-related vasculopathy, long-term follow-up with periodic CTA/MRA is crucial. Additionally, optimizing blood pressure control and considering adjunctive medical therapy may help reduce arterial wall stress and minimize future vascular complications. In our case, although early postoperative imaging confirmed technical success, long-term surveillance remains crucial due to the risk of delayed complications, including graft migration, endoleak formation, and the development of new aneurysms. The patient was scheduled for routine follow-up with CTA at 6 months and annually thereafter to monitor the stability of the repair and assess for potential disease progression. In our opinion, postoperative surveillance should be identical with that suggested from the ESVES guidelines after EVAR, mainly including a yearly imaging evaluation [26].

Conclusions

NF1 patients present distinct challenges regarding treatment of aortic pathology. Although endovascular treatment is not the first choice in these patients presenting with aortic aneurysm or spontaneous ruptures, it may be valuable in urgent cases, even as a bridging procedure, or in redo operations or in high-risk patients. On the other hand, open surgery carries its own risks due

to vascular friability, therefore special care and particular surgical measures are needed.

Funding

No external funding.

Ethical approval

Approval number: 29/11-07-2018.

Conflict of interest

The authors declare no conflict of interest.

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