

**Successful repair of a vasculopathic aneurysmal brachial artery in a patient with
type 1 neurofibromatosis**

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ABSTRACT

Vasculopathy is a well-recognized abnormality associated with neurofibromatosis type 1(NF1) and may cause stenoses, aneurysms and arteriovenous malformations. We report a challenging case of a woman with NF1, who presented with spontaneous rupture of a brachial aneurysm around her right elbow, on a background of previous debulking and soft tissue reconstructive surgery in the same arm. She underwent successful delayed reconstruction of the brachial artery using an autologous great saphenous vein graft.

Keywords: neurofibromatosis type 1, aneurysms, brachial artery.

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INTRODUCTION

Vasculopathy associated with neurofibromatosis type 1 (NF1) has broad phenotypic manifestations including aneurysmal and occlusive disease of large, medium and small arteries.^{1,2} The most common aneurysmal diseases associated with NF1 involve the aorta, renal, mesenteric and carotid arteries. Meanwhile, occlusive diseases most frequently affect the renal arteries, abdominal aorta (coarctation) and mesenteric arteries.^{3,4,5-8} In the context of NF1 other rarer vasculopathies have been reported such as peripheral arterial aneurysms, venous malformations², and extracranial aneurysms of the vertebral arteries⁹.

Despite its rarity, NF1 associated peripheral vasculopathy may have significant clinical sequelae including fatal hemorrhage resulting from aneurysmal rupture.^{8,10-14} Surgical treatment of these aneurysms may prove challenging due to the friable nature of the soft tissues of patients having NF1.^{8,10,14,15} Consequently, the few cases reported in the literature are associated with relatively high mortality and morbidity, including major amputations.^{8,14,15} We present a case of successful delayed repair of an aneurysmal brachial artery in a patient with NF1 presenting with rupture and massive hemorrhage, made more complex by multiple previous debulking and soft tissue reconstructive procedures around the rupture site.

CASE REPORT

A 34 year-old woman, with genetically confirmed NF1 presented with sudden spontaneous onset of severe pain and rapidly progressing swelling and bruising around her right elbow. She was brought to the Accident and Emergency Department within about 3 hours. She had previously undergone extensive plexiform neurofibroma debulking procedures on her right arm on four separate occasions, with complex plastic surgical graft and flap reconstruction over the past 10

years. On detailed questioning, it was clear that there was no previous right upper extremity arterial or venous reconstructions had been required during these procedures. Previously, the extent of NF1 had also been investigated with magnetic resonance imaging (MRI) which did not show involvement of her central nervous system, including her spinal cord, cranial nerves, and optic nerves and chiasma. Over the past 10 years, she had been managing her swollen and deformed right arm by wearing compression garments. She had some degree of impaired motor function of her overall arm.

Her other past medical history included Crohn's disease successfully controlled with Azathioprine and Mesalazine, and mild Factor XI deficiency (Factor XI level of 64 U/dl; normal range 67-149 U/dl) controlled with oral Tranexamic acid prophylactically administered only prior to any surgical procedures. At the time of the initial presentation she was receiving her third cycle of in-vitro fertilisation (IVF) treatment, and was struggling to conceive over the past 3 years.

On clinical examination, she was afebrile and hemodynamically stable. She had a swollen, bruised and deformed right forearm and upper arm associated with extensive scarring from her previous multiple debulking procedures. On palpation, she had a firm, tense and painful swelling on the medial and posterolateral aspect of the right arm in keeping with spontaneous hemorrhage causing a large hematoma. There was no impending compartment syndrome, as the patient had a full complement of upper extremity pulses, with normal capillary refill time and normal sensory function. Neurological examination was unremarkable.

Her blood tests at presentation revealed a significant drop of hemoglobin from 12.2 g/dl to 6.6 g/dl (normal range 12.1 – 15.1 g/dl), an increase of the WBC (white blood cells) to 14.7×10^9 (normal range $4.5-11 \times 10^9$ cells/microlitre), and a mildly raised lactate of 2.5 mmol/L (normal

range 0.5-1 mmol/L). The rest of the blood tests were unremarkable and she tested negative for pregnancy.

Duplex ultrasonography done at initial presentation showed a thrombosed cephalic vein possibly compressed by the large right arm haematoma with a patent deep venous system. A magnetic resonance angiography (MRA) was performed which confirmed a large haematoma within the right arm, surrounding a highly abnormal brachial artery, characterized by tortuosity with two aneurysms. The right innominate, subclavian and axillary arteries were patent and of normal calibre on the MRA (Figure 1).

A diagnosis of acute hemorrhage from her NF1 associated vasculopathy was made although the source of bleeding was not apparent. As the large hematoma was surrounding the brachial artery aneurysms, it was assumed that the haemorrhage arose from the brachial artery aneurysms unless proven otherwise, although other sources of bleeding including from intramuscular and scarred tissue blood vessels remained possible particularly with her past medical history of Factor XI deficiency.

As she was hemodynamically stable and considering the extensively scarred arm with a large hematoma, our initial management decision was to manage the acute rupture by tamponade with compression bandaging; with the intention to surgically explore the arm if the bleeding did not stop or if she became hemodynamically unstable. During this time, we monitored her very closely for any symptoms and signs of compartment syndrome including disproportionate pain, loss of sensation and motor function, increased capillary refill time and absence of pulses which she did not develop. She also received immediate intravenous then oral tranexamic acid and three units of red blood cells transfusion. This therapeutic regimen successfully stopped her bleeding. As a result, we decided to delay the definitive surgical intervention at least until the hematoma had

resolved completely, in an elective setting with adequate patient optimisation and clinical information gathering, unless the aneurysms re-bleed. Emergency surgical exploration of her arm at this time would be very challenging and with high risk due to the presence of the large hematoma, and extensive scarring and friable tissues; potentially leading to life-threatening hemorrhage, limb loss and major nerve injury. Her right arm swelling was managed with elevation using a Bradford arm sling, and physiotherapy. She was discharged home after 13 days from the initial presentation.

It was always our intention to repair the brachial artery aneurysms surgically to prevent them from bleeding again. On resolution of the swelling, her vessels were reassessed using multiple imaging modalities to gain more information about the status of the vessels, the surrounding musculature, soft tissue and the evolution of the hematoma overtime; duplex ultrasonography and MRA were used to screen her entire vascular system, which excluded the presence of other arterial aneurysms (Figure 2).

Eight months after her acute presentation, the hematoma had completely resolved, with right arm swelling at its minimum, leaving the underlying aneurysmal brachial artery, which had increased in size by 1 cm over the period (finding confirmed on the follow-up MRA). A multidisciplinary decision to proceed to definitive surgery was made. As part of the pre-operative work-up for surgery in order to further assess any potential associated arterio-venous malformations, a right upper extremity arteriography and venography were performed; venograms showed widely patent and normal brachial, axillary and subclavian veins. Transfemoral arteriography showed a tortuous proximal brachial artery with two brachial artery aneurysms distally, the larger measuring 38 mm in maximal diameter with no obvious arteriovenous malformations or fistulae (Figure 3C,D).

Definitive elective surgical repair was performed under general anaesthesia. The two brachial artery aneurysms were clamped after heparinisation, then laid open and repaired by brachial-brachial interposition bypass using reversed autologous great saphenous vein (GSV) as a conduit. Prophylactic oral tranexamic acid was administered prior to surgery as a precautionary measure for her Factor XI deficiency. Fresh frozen plasma was used intravenously to aid coagulation during dissection. She received one unit of red blood cell auto-transfusion, recovered from cell salvage.

Proximal arterial control of the distal axillary artery was secured prior to approaching the aneurysmal brachial artery. A lazy-S incision was then made extending from right antecubital fossa to the mid forearm. Distal control of the brachial artery was difficult due to extensive and fragile veins embedded in extremely scarred tissues, the remnant plexiform neurofibroma and the aneurysms. The aneurysmal segment of the brachial artery measured 10 cm in length, and was dissected out to gain proximal and distal control (Figure 4A). A total of 6000 IU of unfractionated heparin was administered systemically prior to clamping. A brachial-brachial artery interposition end-to-end reversed GSV graft was performed; continuous 6/0 Prolene sutures were used for proximal and distal anastomoses (Figure 4B).

On de-clamping, good radial and ulnar pulses were palpable. Her post-operative care was unremarkable. Sensation and motor function of her right upper limb were preserved. Her right arm was gently compressed with wool and crepe bandages and elevated to minimize swelling. She was prescribed right arm physiotherapy. Her check duplex scan and MRA post-operatively demonstrated a patent brachial-brachial vein graft (Figure 5). She remained well at follow-up 1-, 3- and 6- months postoperatively, as clinically there was no impairment of the distal circulation of her right upper extremity and the duplex ultrasonography and MRA did not demonstrate any

aneurysmal recurrence or anastomotic stenosis. As a result of her likely increased risk of true aneurysm and pseudoaneurysm formation, as well as obstructive lesions secondary to her friable tissue from NF1 associated vasculopathy and scarring from previous surgery, her brachial artery would be regularly monitored with duplex ultrasonography and MRA.

DISCUSSION

Neurofibromatosis type 1 (NF1), previously known as von Recklinghausen's disease is a congenital autosomal disease, resulting from a mutation of the NF-1 gene located on the long arm of chromosome 17 (17q11.2).¹⁶ Specific clinical characteristics of NF1 include a wide range of abnormalities ranging from a few nodules or pigmented areas to gross deformity. Typically this disorder includes the presence of cafe-au-lait macules and neurofibromas at an early age, and the diagnosis is made based on a set of criteria set up by the National Institute of Health.¹⁷

Neurofibromatosis is associated with direct tissue invasion causing compression of the vasa-vasorum, and thinning and fragmentation of intima and muscularis media which result in arterial wall weakening and hemorrhage.⁸ Despite multiple previous extensive plexiform neurofibroma debulking procedures with complex plastic surgical graft and flap reconstruction, our patient confirmed that she never had any brachial artery and vein reconstruction that would have led to her abnormal brachial artery. Furthermore, we did not encounter any apparent features of previous vascular reconstruction around the brachial artery including the aneurysms intra-operatively. The fusiform, rather than saccular appearance of the aneurysms also pointed towards non iatrogenic or infective cause of the dilatation. Therefore, we did not perform any histological analysis of the aneurysms as we did not think that it would change our diagnosis and management

since she had been genetically confirmed to have NF1 which was known to be associated with aneurysmal vasculopathy.

Although some authors successfully recreated a vascular conduit using vein graft, many others reported failed reconstruction or adopted salvage procedures such as simple ligation and resection with high mortality and morbidity.^{8,10,14,15} Emori et al.¹⁰ reported a case series of three ruptured aneurysms of the brachial artery that developed in patients with NF1 treated by surgical revascularization. Unfortunately, the outcome was extremely poor with two deaths and one requiring transhumeral amputation due to unsuccessful repair of the brachial artery.^{8,14,15} In the same report, they described the first successful brachial artery reconstruction using a reversed autologous saphenous vein in a woman with plexiform NF1 who presented with a ruptured brachial artery aneurysm. Consequently, because of the extreme vessel wall fragility and the difficulties in obtaining haemostasis, surgical treatment of ruptured aneurysms in NF1 is technically demanding.¹⁰ As a result, very little is known about the natural history of the peripheral arterial aneurysms associated with NF1 and the optimal management in such cases.²

Some investigators recommend that a NF1 related aneurysm might be better treated by an endovascular approach (including stenting or embolization) or a hybrid procedure, rather than by surgery alone, providing the distal circulation is preserved.^{9,14,16-18} However, in our case an endovascular option was not considered because of the extreme tortuosity and fragility of the brachial artery, as any stress on the arterial wall, including the repeated trauma from a wire and stent deployment would have been likely to cause injury.

It is controversial whether routine screening for vasculopathy is indicated in asymptomatic patients with NF1 because of its low incidence.¹⁰ However, if there is clinical suspicion of vasculopathy, selective imaging (magnetic resonance angiography or computer tomography

angiography) of the head, chest and abdomen is justifiable because of the multiplicity of lesions in some patients.² Our patient had not been previously screened for vasculopathy, and the pre-operatively vascular assessment of our patient did not reveal any additional vascular abnormalities.

With regards to the delayed decision in providing surgical correction of the brachial aneurysms, multi-disciplinary meetings and the patient agreed that an elective definitive surgery to exclude the brachial artery aneurysms by interposing a reversed segment of the great saphenous vein would be needed before the aneurysms rupture. However, it was considered that the definitive surgery would be safest when the haematoma had fully resolved and the right arm swelling was at its minimum, and with optimal haematological support for her potential bleeding risk from her mild Factor XI deficiency. Therefore, she was followed-up closely in the Vascular Malformation, Haemophilia, and Neurofibroma Specialist Clinics following discharge, including to monitor her right arm swelling and preparation for potential near future definitive treatment for her brachial artery aneurysms.

Our case report does not recommend that pressure tamponade and medical therapy to be the mainstay treatment for all patients with a potential rupture of NF1 associated arterial aneurysm. Emergency operative intervention should remain the mainstay treatment for rupture NF1 associated arterial aneurysm particularly in patients who are actively bleeding or hemodynamically unstable. Fortunately, in our case, the bleeding was successfully stopped with pressure tamponade which was initially applied with the intention to only temporarily control the bleeding. There was also the possibility of the hematoma could have arisen from other sources of hemorrhage including a rupture intramuscular or scarred tissue blood vessels. However, with a large hematoma surrounding the two brachial aneurysms, it was important to assume that the bleeding was due to the aneurysms until proven otherwise. It is also important to stress that tamponade pressure with

compression bandaging on a hematoma in the upper limb could increase the risk of compartment syndrome. Therefore, in this case, we closely monitor the patient for symptoms and signs of compartment syndrome which she did not develop.

Surgical intervention in this case was indeed very risky, more so if it was done in the emergency setting with large hematoma, and inadequate imaging information and optimization of the patient. However, despite the success of our initial non-operative management, it was always our intention to repair the brachial artery aneurysms eventually to prevent future life-threatening bleeding again. It was thought that surgical intervention was best done when the hematoma had resolved completely in an elective setting. Multi-disciplinary planning with adequate information and investigations was also deemed important. It took 8 months for the hematoma to adequately resolve during which we monitored the patient closely. During this time, we also performed all clinical information gathering including investigations, and subsequently the definitive surgical decision and plan were made through a multi-disciplinary team approach involving the vascular surgeons, interventional radiologists, neurologists with interest in neurofibroma, anaesthetists, and hematologists.

A decision to perform the definitive surgery was made eight months after the acute episode when the haematoma had completely resolved, with the right arm swelling at its minimum; although the brachial artery aneurysms were asymptomatic, investigations have revealed a significant increase in size over the period, which has indicated the surgical correction. The brachial aneurysms were therefore successfully excluded and patient was clinically monitored at 1 month, 3 months and 6 months post-operatively, and the Duplex scans and MRA have confirmed the patency of the graft and eliminated aneurysmal recurrence.

CONCLUSION

From review of the literature, this is only the second case report of successful reconstruction of a ruptured brachial artery aneurysm associated with NF1. In addition, this case was further challenged by the significant overlying scar tissue and residual neurofibromata at the site of the operation from previous debulking and plastic reconstructive procedures, as well as the patients Factor XI deficiency and the recent administration of IVF related drugs, further increasing the risk of bleeding. During the acute episode, our case was successfully managed non-operatively by resuscitation, and compression and elevation of the bleeding brachial artery aneurysm. This perhaps contra-intuitive approach proved an effective bridge to definitive resection and reconstruction, undertaken in an elective setting, in the absence of hemodynamic compromise, utilizing all precautionary measures, and once the local swelling and hematoma had settled.

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Figure 1 - Initial MR angiography of the right upper extremity shows normal subclavian and axillary arteries and a tortuous proximal brachial artery, with 2 brachial aneurysms distally, with the largest measuring 28 mm (*arrows*), followed by the tortuous radial and interosseous arteries.



Figure 2 - MR angiography of the whole body at 2 months follow-up demonstrates no significant aortic, visceral, renal or iliac arterial abnormality, with patent central veins, superior and inferior vena cava and iliac veins.

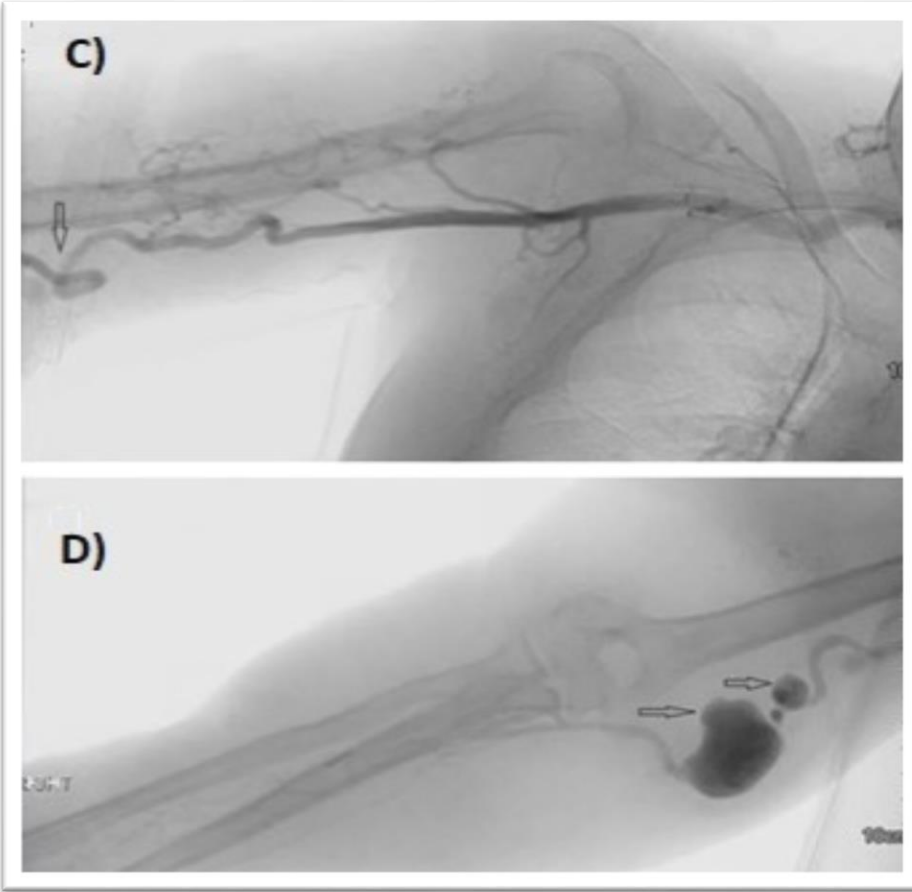


Figure 3. **C)** Transfemoral catheter arteriography of the right upper limb shows the normal subclavian and axillary arteries with the abnormal proximal brachial artery, characterised by tortuosity (*arrow*). **D)** The arteriogram demonstrates two brachial artery aneurysms, the largest measuring 38 mm (*arrows*), then trifurcating into a normal ulnar artery and tortuous radial and interosseous arteries.

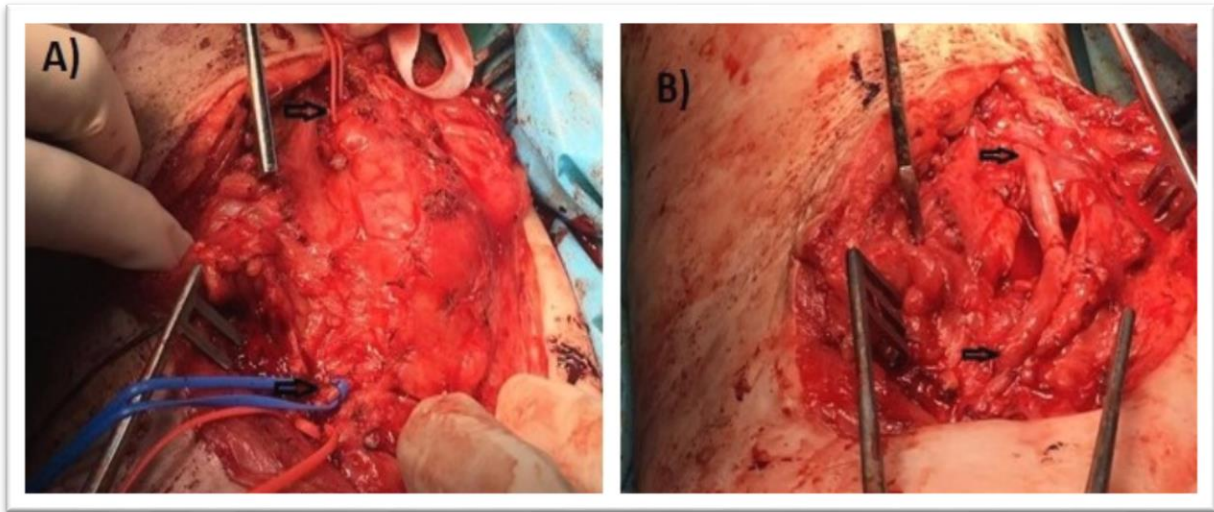


Figure 4 – intraoperative images:

- A. Intraoperative photograph shows the in situ large brachial artery aneurysm, with the proximal and distal non-aneurysmal segments of the brachial artery dissected out and controlled with vessel-loops (*arrows*).
- B. Intraoperative photograph shows the brachial-brachial artery interposition using the reversed great saphenous vein conduit, with the proximal and distal anastomosis (*arrows*). There was mild discrepancy in terms of the diameter between the great saphenous vein graft and the distal brachial artery although subsequent follow-up duplex ultrasound scan did not show any flow restriction.

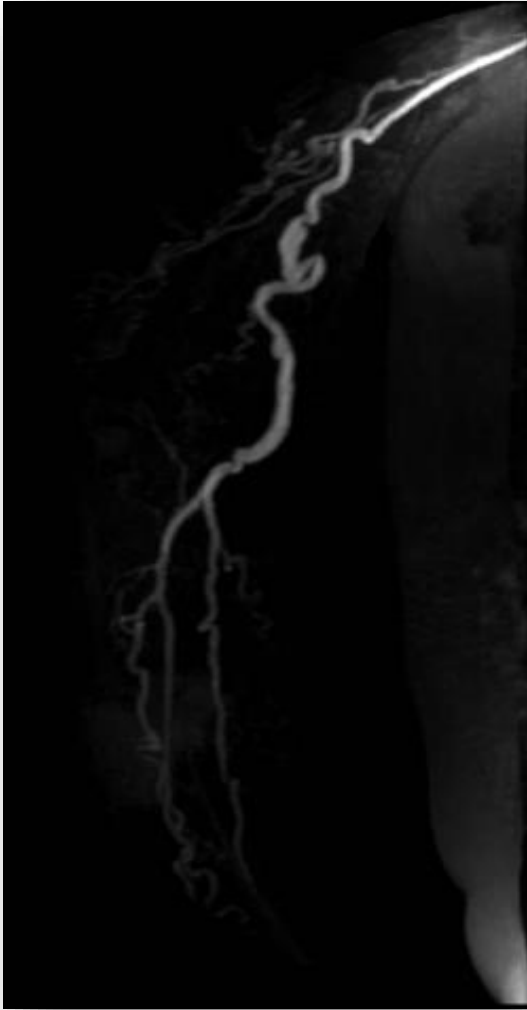


Figure 5 – post-operative follow-up at 6 months –showed patent interposition graft, mild distal anastomosis stenosis, but irrelevant clinically, with preserved distal circulation.