Case Report

# Neurofibromatosis Type 1 and Renal Artery Aneurysms: An Uncommon Entity of Severe Hypertension

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Neurofibromatosis (NF1) is a relatively common autosomal dominant disorder. Secondary causes of hypertension, such as renovascular disease, coarctation of the abdominal aorta or phaeochromocytoma, may be identified in up to 1% of patients with NF1. Usually, renal angiography, which is always used to confirm the diagnosis of renovascular hypertension, reveals stenoses and rarely bilateral or unilateral renal artery aneurysms. We present the first description of a percutaneous transluminal renal angioplasty performed in an adult female patient with NF1, severe hypertensive disease and renal artery aneurysms, in order to restore renal artery anatomy and treat renovascular hypertension.

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Neurofibromatosis type 1 (NF1; von Recklinghausen disease) is an autosomal dominant disorder with complete penetrance, variable expression and a frequency of 1:3000.[1] However, approximately 50% of cases result from spontaneous mutations. This hamartous disorder arises from the neural crest, involving ectodermal, neuroectodermal and mesodermal tissue. The incidence of secondary hypertension in NF1 is approximately 1%, as a result of coarctation of the aorta, phaeochromocytoma or renal artery stenosis, and rarely renal artery aneurysms.[2] We present the first description of a percutaneous transluminal renal angioplasty performed in an adult female patient with NF1, severe hypertensive disease and renal artery aneurysms in order to restore renal artery anatomy and treat renovascular hypertension.[2]

## Case presentation

A 28-year-old woman came to the emergency room with a severe headache. She mentioned that she had measured high blood pressure (230/130 mmHg) a couple of weeks earlier, while her family history for hypertension or cardiovascular disease was unremarkable.

On physical examination, multiple café-au-lait spots ≥5 mm were revealed, spread over the skin of the trunk, while numerous small nodules ≤5 mm were palpable in the abdominal area (Figure 1). Biopsy of the skin lesions revealed the diffuse type of NF1, which was confirmed by the immunopositivity of many tumour cells for S100 protein (Figure 2). Her cardiovascular examination was near normal (no cardiac murmurs or abdominal bruits, normal ECG, mild left ventricular concen-

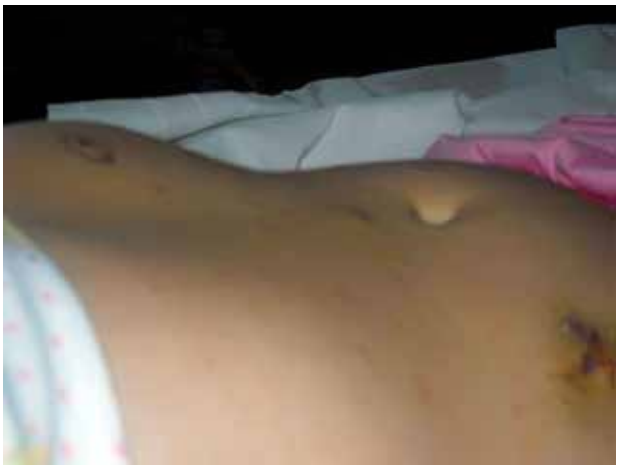

**Figure 1.** Numerous small palpable nodules with a diameter ≤5 mm in the abdominal area.

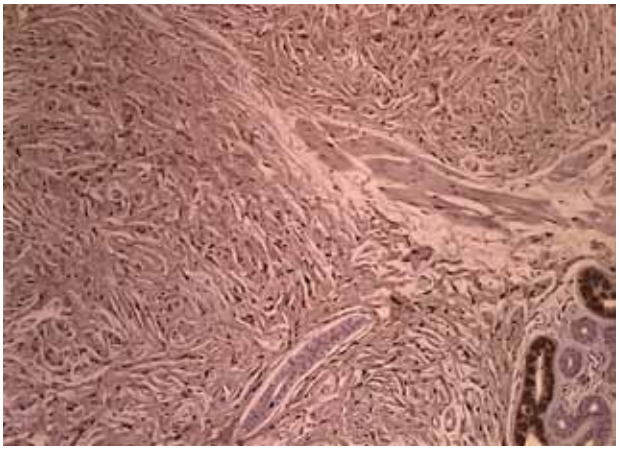

**Figure 2.** Biopsy of the skin lesions revealed the diffuse type of neurofibromatosis type I, which was confirmed by the immunopositivity of many tumour cells for S100 protein.

tric remodeling on echocardiography). Funduscopic examination revealed bilateral hypertensive retinopathy stage III-IV. No Lisch nodules were found. Computed tomography of the brain was within normal findings.

Since 24-hour urine levels of catecholamines, metanephrines and vanillylmandelic acid, and magnetic resonance imaging of the adrenal glands were all normal, we further investigated the possibility of renovascular hypertension. Indeed, renin (45.1 μU/ml and 64.9 μU/ml) and aldosterone levels (661 pg/ml and >2000 pg/ml) were increased both at rest and during stress, respectively, while magnetic resonance renal angiography revealed two large aneurysms of the left renal artery separated by an arterial segment of nearly normal diameter, which could act as a stenotic lesion (Figures 3A & 3B) and renal Tc 99-m DTPA scintigraphy with a captopril test suggested an intermediate risk for renovascular hypertension (Figure 4). Intensive antihypertensive treatment led to blood pressure normalisation. Since the patient refused surgical therapy, and in order to treat the hypertension and reduce the risk of rupture of the an-

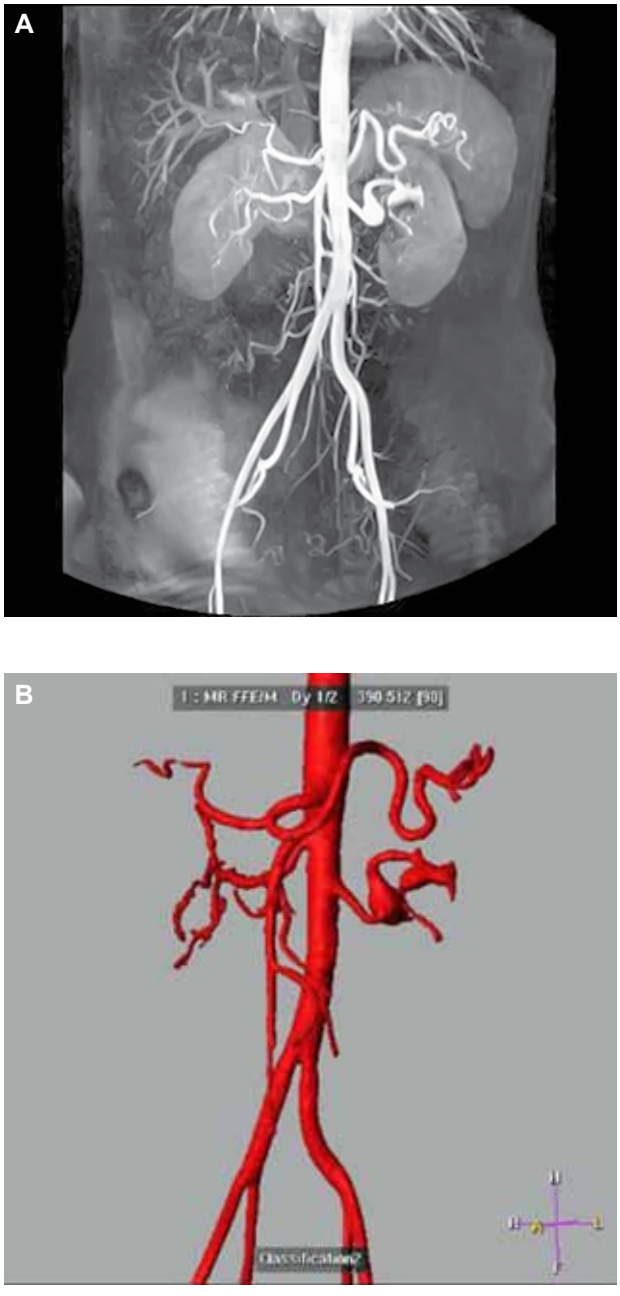


**Figure 3.** Magnetic resonance renal arteriography (A) and 3D reconstruction of the renal arterial bed (B), which revealed two large aneurysms of the left renal artery separated by an arterial segment of nearly normal diameter.

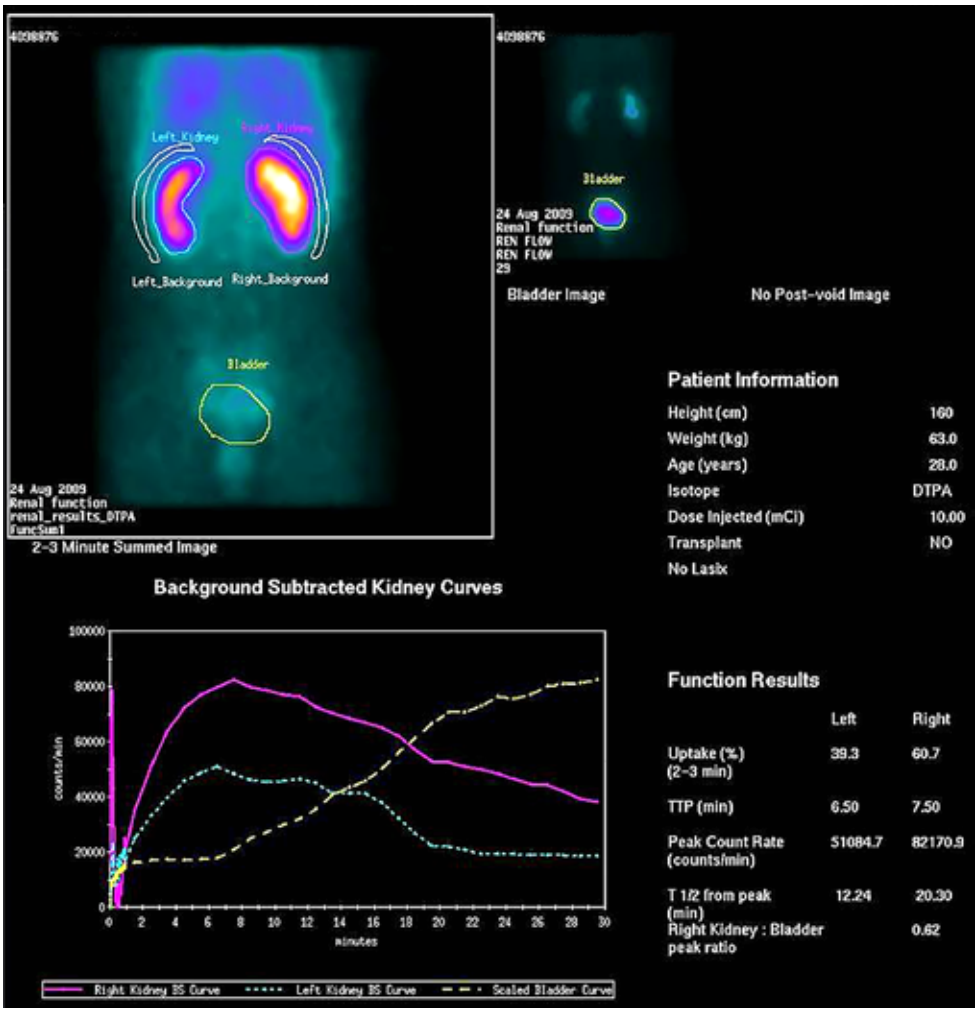


**Figure 4.** Pre-procedure (renal angioplasty) renal Tc 99-m DTPA scintigraphy with captopril test. Left kidney function (39%) was decreased compared to the right kidney (61%).

eurysms, we decided to restore renovascular anatomy by performing angioplasty of the proximal aneurysm (two covered stents with diameters of 6 mm and 5 mm) and coil embolisation of the distal aneurysm (Figure 5). The procedure was successful and the hypertension was normalised. Unfortunately, when the patient was re-evaluated one month later, her blood pressure was again elevated, while no left kidney function was revealed on renal scintigraphy. The patient refused further evaluation and treatment and she left the hospital.

## Discussion

Neurofibromatosis is an autosomal dominant disorder. Its major feature is the occurrence of multiple neurofibromas, which are benign tumours of the nerve sheath and may affect any organ system.[3] The diagnosis of NF1 is usually based on clinical criteria: café-au-lait spots, which arise in 95% of patients, are flat areas of skin hyper-pigmentation with rounded edges, while their number and size increase during infancy. The typical characteristic of NF1 is the neurofibroma that is revealed within the dermis in 95% of patients. In our patient, NF1 was diagnosed as she had more than six café-au-lait spots (criterion 1) with diameter ≥1.5 cm (criterion 2), and more than two neurofibromas within the dermis (criterion 3).[1]

Six percent of patients with NF1 develop hypertension, either essential hypertension, which is the most common form in adults, or secondary hypertension due to renovascular disease, coarctation of the abdominal aorta or phaeochromocytoma, which may be identified in 1% of NF1 patients. In children, young adults, and often during pregnancy the most common cause of hypertension is renovascular disease, which occurs 7 times more frequently than phaeochromocytoma.[1,3] In contrast to fibromuscular dys-

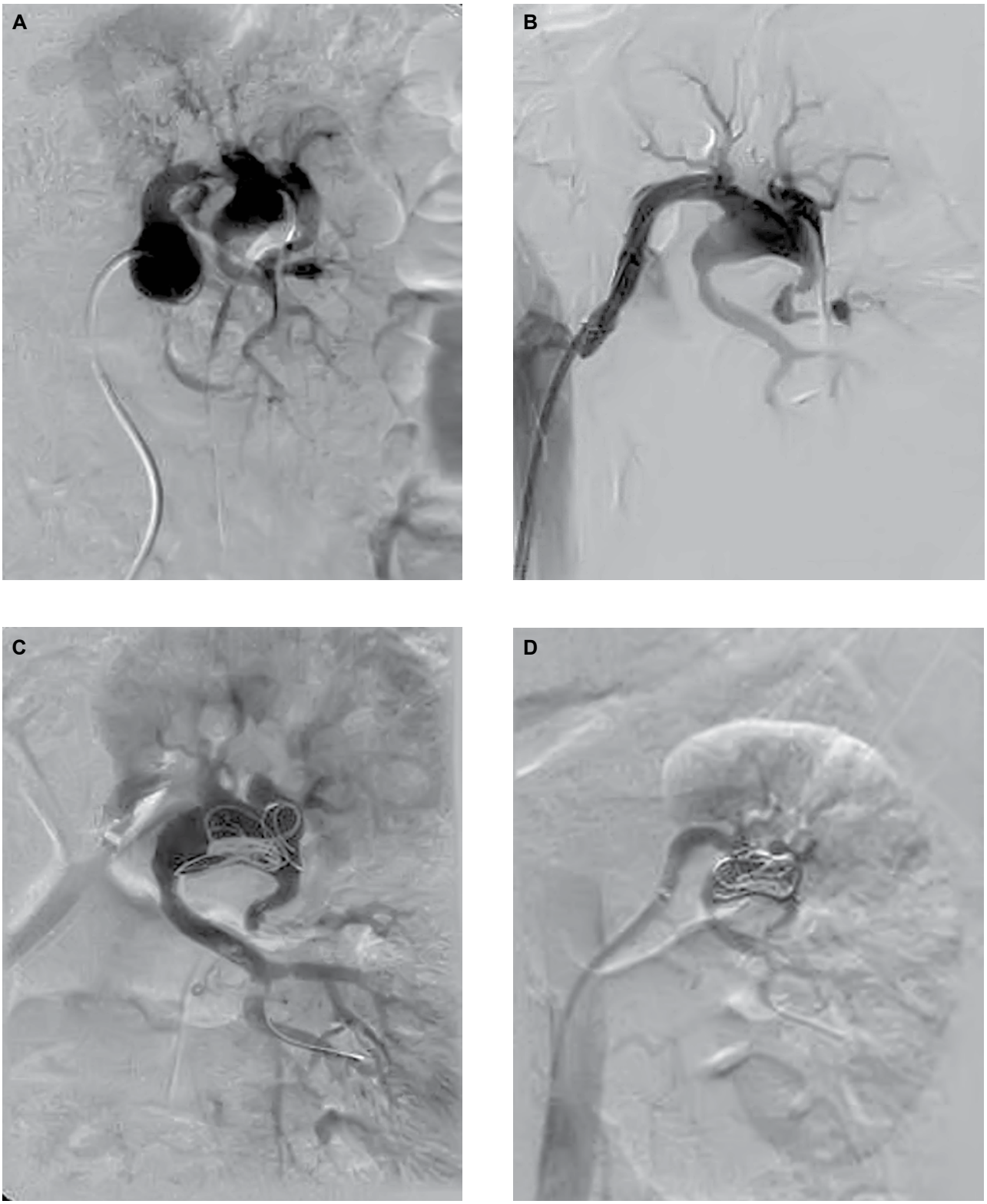


**Figure 5.** Renal artery angioplasty of the proximal aneurysm, before the procedure (A), after the placement of two covered stents (B), after the subsequent coil embolisation of the distal aneurysm (C), and the final result (D).

plasia, where 95% of all stenoses are found in the distal two-thirds of the renal artery, in NF1 more than 50% of all stenoses are located at the ostia.[4] Usually, renal angiography reveals renal artery stenosis followed by post-stenotic aneurysmal dilatation, and rarely bilateral or unilateral renal artery aneurysms.[5-7] In our case, a young woman aged 28 years, coarctation of the abdominal aorta or phaeochromocytoma were excluded. Magnetic resonance imaging of the renal arteries revealed two large aneurysms in the left renal artery, separated by an arterial segment of normal diameter, while the right renal artery anatomy was normal. These results were subsequently confirmed by renal angiography.

The first large series associating renovascular hypertension and NF1 in 10 patients was reported in 1965. All patients had several manifestations of NF1 and involvement of one or both renal arteries, with stenosis or aneurysm or both. The most recent series reviewed 49 patients with NF1 and renovascular hypertension due to renal artery stenoses. Among the associated vascular lesions six renal artery aneurysms were included.[7]

Nuclear medicine has become widely used in the preliminary investigation of young patients with suspected renovascular disease (RAS). However, the captopril challenge test seems inadequate because of its low sensitivity and specificity (59% and 68%, respectively) for diagnosing renal artery stenoses in young populations. It seems that nuclear renography, either with or without captopril, cannot be recommended as a routine investigation for suspected RAS, since the possible coexistence of multiple forms of NF1 vasculopathy (stenoses and/or aneurysms of the renal artery, small renal vessel disease) in any given patient further complicates the interpretation of these diagnostic tests.[3] The diagnosis should always be confirmed by renal arteriography. In our patient, although renin and aldosterone levels were above normal limits, renal Tc 99-m DTPA scintigraphy with a captopril test was inconclusive for renovascular hypertension.

Conservative management seldom results in normalisation of hypertension secondary to renal artery aneurysmal disease, and the majority of patients require endovascular intervention. Treatment of hypertension due to renal artery stenosis and/or aneurysms in NF1 in young patients is usually a combination of drug therapy, percutaneous transluminal angioplasty (PTA) and surgery. Optimal treatment remains highly individualised and requires collaboration between a cardiologist, radiologist and nephrologist, as well as the will of the patient. PTA seems to be suitable for discrete lesions, whereas more extensive renal artery lesions with involvement of intra-renal vessels need surgical revascularisation (reconstructive vascular surgery, embolisation, autotransplantation, partial or total nephrectomy).[8]

Han and Criado reviewed 49 patients with NF1 and renovascular hypertension, aged 4 months to 34 years (mean 11 years). Eight of these patients were treated with medication alone, 10 had a nephrectomy, 13 had surgical revascularisation procedures, 16 had a PTA and 1 had transluminal embolisation of a renal artery aneurysm. Hypertension was cured in 56% of patients treated with surgery and in 59% of patients treated with PTA, and improved in 56% of patients receiving medication alone. However, no sufficient data regarding the long-term follow up were provided for those patients who were treated successfully with PTA.[7]

Success rates for PTA at a tertiary centre prior to any surgical intervention are 33%. A further 20% of patients benefit from an improvement in blood pressure control.[4] Potential complications of PTA are both local at the puncture site and major, such as embolisation of the kidney, renal infarction, dissection, perforation or rupture of the renal vasculature, and transient renal failure induced by contrast media.[4] However, acute renal insufficiency due to automatic renal infarctions has been described in the past as a complication of neurofibromatosis.[9]

To our knowledge, this is the first description of a percutaneous transluminal renal angioplasty performed in an adult female patient with NF1, severe hypertension disease and renal artery aneurysms, in order to restore the renal artery anatomy and treat renovascular hypertension. The reproductive age of the patient demanded a non-conservative approach, since antihypertensive treatment had to be avoided and complications such as worsening of hypertension or eclampsia later during a possible pregnancy had to be prevented.[10] PTA with stent placement and coil embolisation of the distal renal aneurysm was initially effective, since the patient's blood pressure decreased to within normal limits, less antihypertensive medication was needed, and kidney function remained normal. Unfortunately, the procedure was complicated, the function of the left kidney was lost, and blood pressure later increased again, possibly because of embolisation of the kidney and/or renal infarction. The patient refused further management as well as genetic counselling and she decided to leave the hospital.

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