

## Case Report

# Hypertension secondary to renal vasculopathy in an adolescent with neurofibromatosis type 1: a case report

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**Abstract:** Neurofibromatosis type 1 (NF-1) is a nerve and skin disease that involves an autosomal dominant mutation in the NF-1 gene on chromosome 17. NF-1-induced vasculopathy is an important condition that is usually fatal, but it is often overlooked, especially in children. Secondary causes of hypertension, such as renovascular disease, coarctation of the abdominal aorta, or pheochromocytoma, may be identified in up to 1% of patients with NF-1. We report the case of a 14-year-old boy with NF-1 who developed hypertension due to stenosis and an aneurysm located in his left renal artery. He had approximately 20 café-au-lait spots on his abdomen, back, and arms. His father also had café-au-lait spots on his back. Aortography and a selective left renal angiogram revealed 80% stenosis and an aneurysm in his left renal artery. In conclusion, we report on an NF-1 patient who developed hypertension secondary to renal artery stenosis and an aneurysm. This case demonstrates the importance of a detailed examination, including blood pressure, in children with NF-1.

**Keywords:** Hypertension, renal artery stenosis, aneurysm, neurofibromatosis type 1

## Background

Neurofibromatosis type 1 (NF-1) was first described by Von Recklinghausen in 1882 and is an autosomal dominant disease that occurs with a frequency of approximately one in 3000 live births [1, 2]. The incidence of secondary hypertension in NF-1 is approximately 1%, and is a result of coarctation of the aorta, pheochromocytoma, renal artery stenosis, or rarely renal artery aneurysms [3, 4]. Here, we report a case of hypertension caused by left renal artery stenosis and an arterial aneurysm in a 14-year-old boy with NF-1.

## Case presentation

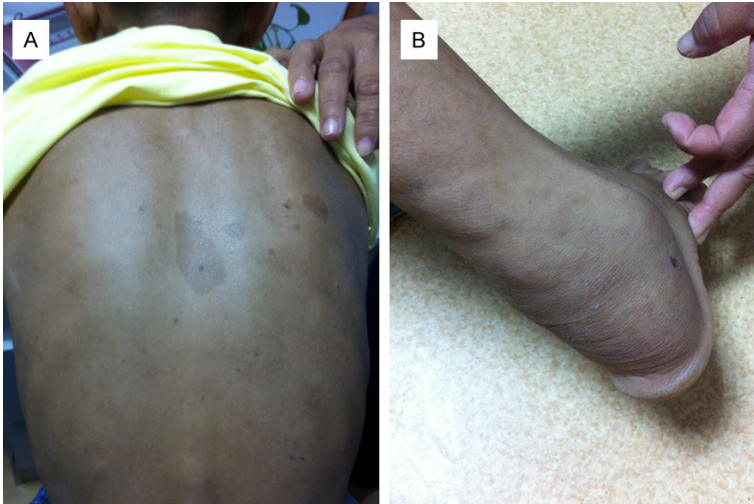
A 14-year-old boy presented with a 2-year history of minor headache at his temples with no nausea or vomiting. He had intermittent headaches approximately twice a month lasting a few hours. He had approximately 20 café-au-lait spots over his abdomen, back, and arms. His father also had café-au-lait spots on his back.

On admission to the hospital, he was well, but his blood pressure was 190/140 mmHg in his

arm. He had more than six café-au-lait spots and the largest on his back measured 6×3 cm (**Figure 1A**), while the smallest (0.5×0.5 cm) was on his abdomen; he had one plexiform neurofibroma 10×6 cm in diameter on his right ankle (**Figure 1B**).

His renal function was normal. The vanillylmandelic acid excretion was normal and echocardiography showed mild left ventricular hypertrophy and no structural abnormality. A renal ultrasound showed two normal kidneys. A renal angiogram showed an aneurysm of the left renal artery (**Figure 2**). Aortography and a selective left renal angiogram revealed 80% stenosis of the left renal artery before the aneurysm. The right renal, coeliac, and superior mesenteric arteries appeared normal. Cranial magnetic resonance imaging (MRI) showed abnormal long T1 and T2 signals in the area of the basal ganglia bilaterally (**Figure 3**). Both the patient and his parents refused percutaneous transluminal renal angioplasty (PTRA). Nifedipine treatment was continued and the patient was followed as an outpatient with close monitoring of his blood pressure and renal function at least once every 3 months. PTRA was kept as

## Hypertension due to a renal artery aneurysm and stenosis in NF-1



**Figure 1.** Multiple café-au-lait spots on the patient's body (A) and a large mass on the right ankle (B).

an option should the patient's condition deteriorate. The blood pressure at the 1-year follow-up was controlled at 160/90.

### Discussion

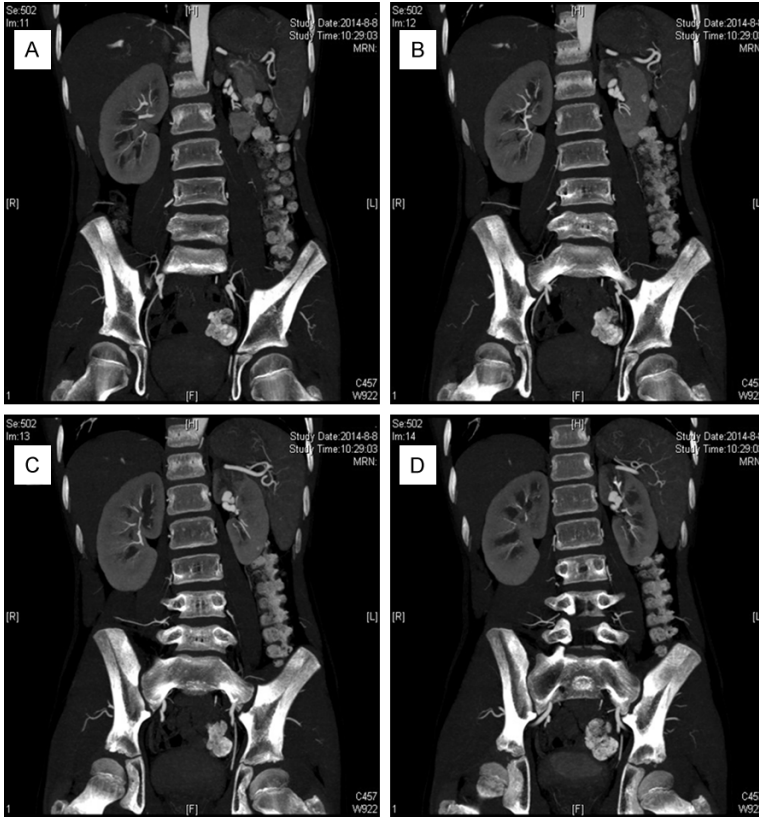
We report the case of a 14-year-old boy who presented with hypertension. He was diagnosed with NF-1, unilateral renal artery stenosis, and a renal artery aneurysm. In 1988, the National Institutes of Health established diagnostic criteria for NF-1, which are satisfied when two of the following are present [5]: café-au-lait spots on the skin ( $\geq 6$  spots  $> 5$  mm before puberty or  $> 15$  mm after puberty); intertriginous freckling (axillae, groin, and neck); dermal neurofibroma ( $\geq 2$ ); optic pathway glioma; iris hematoma (Lisch nodules); skeletal dysplasia (tibial or sphenoid wing dysplasia); and a positive family history of NF-1 affecting a first-degree relative. Café-au-lait spots, which are present in all patients, may be the only feature apparent in some patients, especially infants and children. In our patient, NF-1 was diagnosed because he had more than six café-au-lait spots with diameters  $\geq 1.5$  cm and Lisch nodules.

The cardiovascular features of NF-1 include congenital heart disease, vasculopathy, and hypertension. Vasculopathies are the second leading cause of death in NF-1 [6]. Hypertension ( $> 95^{\text{th}}$  percentile for age and gender) in children with NF-1 is mostly due to renal artery stenosis, followed by coarctation of the aorta and pheo-

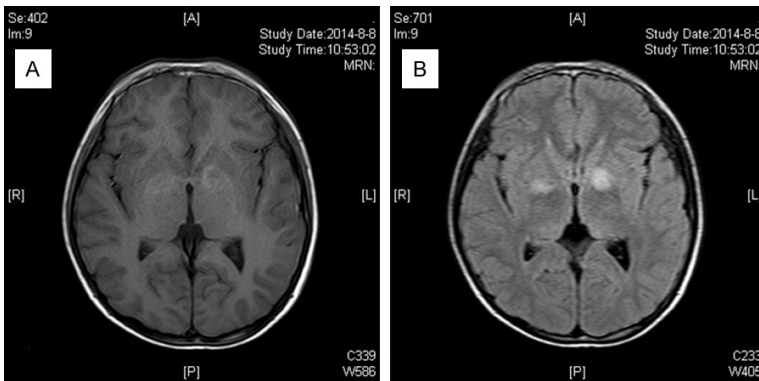
chromocytomas [7]. Vascular abnormalities are rare complications of NF-1 and include renal, aortic, and mesenteric stenosis and affect approximately 2% of patients [8]. The most common site of vasculopathy is the renal artery, accounting for approximately 41% of the cases of NF-1 vasculopathy [9]. Renal artery stenosis typically affects the origin of the vessel and may be associated with stenosis in other vessels. Rarely, an aneurysm and stenosis can occur simultaneously in the same large artery in NF-1. We report a case of hypertension caused by left renal artery stenosis

together with a renal artery aneurysm in a 14-year-old boy with NF-1. In this case, imaging showed no signs of pheochromocytoma, but did show left renal artery stenosis and aneurysm.

Greene *et al.* described two histological characteristics of the vessels in neurofibromatosis: one involves larger vessels (aorta, proximal renal arteries, and carotid arteries) and the other smaller, more peripheral ones [10]. In the former, the vessels may be surrounded by neurofibromatous or ganglioneuromatous tissue in the adventitia. There is intimal proliferation, thinning of the media, and fragmentation of the elastic tissue. In the latter, there are no associated neural malformations and Greene *et al.* speculated that there was dysplasia of the small vessels [11]. However, the two histological findings may coexist and in some instances the vascular abnormality may be widespread and involve arteries, arterioles, and veins in the kidneys. Greene's hypothesis may explain the renal artery vasculopathy seen in our patient with NF-1. The NF-1 gene affected the large vessels, with intimal proliferation and thinning of the media, which caused the stenosis of the left renal artery stenosis. The gene affected the vessels causing dysplasia and fragmentation of the elastic tissues, which caused the renal artery aneurysm. The characteristic vascular lesions in neurofibromatosis consist of stenotic, proliferative nodules of spindle cells with a marked increase in the mucoid matrix, and



**Figure 2.** The aneurysm in the left renal artery on enhanced computed tomography.



**Figure 3.** Abnormal signals in the bilateral basal ganglia on T1- and T2-weighted flair MRI.

thinning and loss of media and elastic lamina, which lead to aneurysm formation [12]. In our patient, it is not clear whether the stenosis or the aneurysm was the primary lesion or if these two lesions developed simultaneously.

Conservative management seldom results in normalization of hypertension secondary to renal artery aneurysmal disease, and the ma-

jority of patients require endovascular intervention [13]. The treatment of hypertension due to renal artery stenosis or aneurysms in NF-1 in young patients is usually a combination of drug therapy, PTR, and surgery. However, only 33% of pediatric patients with NF-1 showed blood pressure improvement after PTR [14]. Our patient and his family refused PTR for financial reasons.

### Conclusion

In summary, we report on a NF-1 patient who developed hypertension secondary to renal artery stenosis and an aneurysm. Our case demonstrates the importance of a detailed examination, including blood pressure, in children with NF-1. Patients with neurofibromatosis and hypertension should be screened for pheochromocytoma and renovascular hypertension. Wider awareness of NF-1 is warranted to enable an early diagnosis and prompt, appropriate treatment. All young patients with hypertension should be screened for secondary causes of hypertension, including NF-1, so that renal revascularization can be offered before permanent end-organ damage has occurred.

### Disclosure of conflict of interest

None.

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