Case Report

Neurofibromatosis and renovascular hypertension presenting in early pregnancy

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Introduction

Neurofibromatosis is a hamartomatous disorder of neural crest tissue transmitted in an autosomal dominant manner [1]. In neurofibromatosis there is an increased incidence of hypertension due to phaeochromocytoma, coarctation of the aorta, and a number of vascular abnormalities, which may produce renovascular hypertension [1]. These include renal artery stenosis [2], saccular aneurysm formation and intrarenal parenchymal vessel abnormalities [3] that can lead to chronic ischaemia and fibrosis. Most cases of renovascular hypertension associated with neurofibromatosis have presented in childhood [4,5]. Pregnancy in individuals with neurofibromatosis has been associated with a high incidence of gestational hypertension and pre-eclampsia as well as the possibility that the vascular lesions of neurofibromatosis may be induced or aggravated by pregnancy [6–8]. We present a case of severe renovascular hypertension complicating pregnancy in a 26-year-old woman with neurofibromatosis.

Case report

A 26-year-old woman with neurofibromatosis was referred for investigation and management of her severe hypertension at 17 weeks gestation. Blood pressure on presentation was 240/140 despite therapy with labetalol 400 mg twice daily and α-methyladrenergic 500 mg four times daily. This was not associated with any evidence of end-organ damage and clinical examination demonstrated the cutaneous manifestations of neurofibromatosis but was otherwise normal. In her past history at the age of 16 she had been investigated by the hypertension clinic who had screened for a phaeochromocytoma but had not investigated the renal vasculature. She was subsequently lost to follow-up.

Routine biochemistry and haematology were normal. There was no significant proteinuria. Subsequent investigations demonstrated normal plasma catecholamines but a markedly elevated plasma renin activity (23.8 nmol/l/h, normal 0.15–1.55 nmol/l/h) and plasma aldosterone at 2386 pmol/l (normal 140–550 pmol/l) consistent with renal ischaemia. Doppler ultrasound studies were technically difficult because of the pregnant uterus, but no obvious abnormalities were noted. Specifically there was no evidence of coarctation of the aorta.

The patient’s blood pressure was controlled on a regime of hydralazine (200 mg daily), labetalol (1200 mg daily), and α-methyladrenergic (4000 mg daily). Average blood pressure recordings were 150/90. Low-dose aspirin was also used as a possible prophylaxis against the development of pre-eclampsia.

A caesarean section was performed at 28 weeks gestation for poor intrapartum growth and abnormal CTG tracings (deceleration and poor reactivity), with the delivery of a male infant weighing 870 g. The child is alive and well but has cerebral palsy. Postpartum blood pressure was well controlled, in a normal range, with lisinopril 10 mg daily and amiodipine 10 mg daily.

The patient was readmitted 3 months later for further investigations. Lisinopril was stopped for 1 week prior to admission and blood pressure controlled on amiodipine alone. Renal angiography demonstrated an intrarenal aneurysm in the upper pole of the left kidney with poor perfusion of the upper two-thirds of the kidney (Figure 1). Selective renal-vein renins confirmed the left renal ischaemia. Plasma renin activity from the left renal vein measured 8.7 nmol/l/h compared to the right renal vein and IVC of 4.3 nmol/l/h. The ratio being 2:1. CT scan of the abdomen demonstrated normal adrenals with no evidence of a phaeochromocytoma. The vascular malformation in the left renal artery, demonstrated on angiography, was clearly evident.

A radical left nephrectomy was performed with subsequent normalization of blood pressure immediately postoperatively. Two years later the patient is...
well, normotensive, on no medication, and is contemplating another pregnancy.

Histology

The kidney weighed 88 g, with a mass of vessels of various calibres and tortuosity evident at the hilum. The wall of the renal artery was expanded by fibroblastic cells and hyaline fibrous tissue with dystrophic calcification. The lumen was occluded by an area of spindle-cell proliferation admixed with foamy macrophages and haemosiderin deposits. The spindle cell immunoperoxidase stains were negative for both actin and S100. Many of the vessels showed indeterminant features and were not clearly of venous or arterial origin, consistent with a vascular malformation (Figure 2a). No neurofibromatous tissue was seen. The renal parenchyma showed relatively uniform glomerulosclerosis and tubular atrophy in the superficial region of the cortex consistent with ischaemic atrophy. There was no evidence of hypertensive vascular change.

Discussion

Secondary hypertension may develop with neurofibromatosis by one of two mechanisms, which show an important difference in age incidence. Phaeochromocytoma is the more frequent cause of hypertension in individuals over 18 years of age. Renal artery stenosis is 7 times more likely in the younger age group less than 18 years of age [9,10]. The histology of this case is supportive of a long-standing lesion which may
well have been present at her initial presentation to the hypertension clinic at the age of 16, but renal angiography was not then performed.

The arterial lesions associated with neurofibromatosis have been classified into two basic categories: adventitial neurofibromas or ganglioneuromatous tissue, which involve the aorta and its major branches and may subsequently lead to stenosis or aneurysm formation, and small-vessel lesions, which include concentric proliferation of intimal cell, aneurysmal lesions, and fusocellular nodules between the media and adventitia [3,11,12]. Vascular neurofibromatosis involves the major vessels as well as the smaller intrarenal vessels [13]. Immunohistochemical studies and electron-microscopy have shown that the proliferating spindle cells of the small renal vascular lesions are of smooth-muscle origin [3,11,14].

In this case, the small tortuous hilar vessels showed intimal proliferation of spindle cells with positive staining for actin, suggestive of smooth muscle cell differentiation. This was not evident in the main renal arterial lesion, possibly due to superimposed accelerated atherosclerotic-like changes. No intimal proliferative lesions in the small intrarenal parenchymal vessels were seen. This may be an important and favourable prognostic feature, as the intrarenal arterial lesions can be progressive, occur bilaterally [14], and may be a factor in the failure to alleviate permanently the hypertension, as has been documented in some surgically corrected cases of renal-artery stenosis in neurofibromatosis [2,13].

In the presence of renovascular lesions medical therapy to control the hypertension is usually less successful. In the paediatric setting, Elias et al. [15] reviewed 50 cases of renovascular hypertension associated with neurofibromatosis in children and found that the hypertension in these cases was resistant to standard medical therapy. There are no published series in adults. In this case the hypertension was clearly related to the ischaemic left kidney, as documented on angiography, and with the high renal levels. Initially the patient’s blood pressure was well controlled with an angiotensin-converting enzyme inhibitor (ACEI) and a calcium-channel antagonist. However, surgery was the preferred form of management, because of the unilateral nature of the lesion and the individual’s desire to have further children. Also a fatal rupture of the renal artery caused by a dissecting aneurysm in a pregnant woman with neurofibromatosis has been reported [16].

Although in the older age group phaeochromocytoma is the more likely cause of secondary hypertension in individuals with neurofibromatosis, renal artery lesions must not be overlooked. The patients mostly affected are adult females and the lesions come to light during pregnancy [17]. We would recommended that renal angiography is essential in the investigation of patients with neurofibromatosis and hypertension. In addition, as part of the counselling of an individual with regard to pregnancy and neurofibromatosis, they should be made aware of the increased risk of gestational hypertension and pre-eclampsia. Any hypertension should be investigated before conception, where possible.

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References


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