Renovascular hypertension in neurofibromatosis

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Summary: We present two patients with renovascular hypertension in association with neurofibromatosis. In both cases the diagnosis was established by angiography. The first patient suffered occlusion of the right renal artery combined with intrarenal arterial lesions. Treatment was by autotransplantation. The second patient suffered bilateral intrarenal arterial lesions alone and was treated medically. In both patients, control of the hypertension was established. We discuss the aetiology of renovascular hypertension in neurofibromatosis and consider its treatment.

Introduction

Although hypertension in neurofibromatosis is most commonly essential, the incidence of phaeochromocytoma, coarctation of the aorta, and renovascular hypertension is increased in these patients, the latter occurring in less than 1% of patients with neurofibromatosis.¹ We describe the diagnosis and management of two such patients.

Case reports

Case 1

A 14 year old boy with moderate learning difficulties presented following a grand mal convulsion and was found to be hypertensive with a blood pressure of 160/115 mmHg in both arms. In early childhood *café au lait* macules and macrocephaly had been noted and a diagnosis of neurofibromatosis considered but the family history was negative. By 14 years he had developed axillary freckling and several plexiform neurofibromas and a clinical diagnosis of neurofibromatosis was made. Further examination of the cardiovascular system revealed no abnormality and there were no stigmata of hypertension. An electrocardiogram and a chest X-ray were unremarkable; blood urea, electrolytes and creatinine were all normal. Urinary vanillo-mandelic acid was not raised and renin levels on selective venous sampling were normal.

Ultrasound showed normal sized unobstructed kidneys; an intravenous urogram showed a slightly dense nephrogram on the right which raised the suspicion of a renal artery stenosis. Arteriography

showed a normal vascular pattern on the left, but a short occlusion at the origin of the right renal artery with distal filling of this vessel by collaterals from the lumbar arteries (Figure 1).

A trial of captopril did not produce a satisfactory reduction of blood pressure, and consequently surgical exploration of the right kidney was undertaken. At operation no extrinsic compression of the renal artery was found. The renal artery was divided distal to the stenosis, the kidney autotransplanted into the right groin, and a renal biopsy taken. A post-operative DTPA scan revealed good perfusion of the autograft and the hypertension rapidly settled.

The patient currently remains well with a blood pressure of 110/65 mmHg without any antihypertensive treatment some 12 months later.

Histological examination revealed a striking abnormality of the intra-renal arteries and arterioles which showed marked hypercellularity of the walls giving the appearance of a benign proliferative hamartomatous malformation (Figure 2). The proliferating cells arose from the intima and/or media and formed either a uniform circumferential proliferation or a nodular eccentric proliferation with compramisation of the lumen. Special stains, including immunohistochemistry were not helpful in identifying the histogenesis of these cells. The abnormalities observed were typical of the entity known as vascular neurofibromatosis.

Case 2

A 21 year old woman from Oman, with the cutaneous features of neurofibromatosis, was investigated for severe hypertension of 4 years duration.

On examination there were dermal neurofibromas, *café au lait* patches and axillary freckling. Her blood

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Accepted: 6 July 1988

Figure 1 Selective injection into the first right lumbar artery (a) showing extensive collaterals feeding into the main renal artery (b) via the capsular and adrenal branches (c). The site of the occlusion of the renal artery is marked (d).

Figure 2 Photomicrograph of renal biopsy (haematoxylin and eosin stain; $\times 240$) showing glomerulus (g) with arteriole (a) at pole. The wall of the arteriole is markedly hypercellular due to proliferation of intimal/medial cells.

pressure was 230/130 mmHg in the supine position in both arms with no radiofemoral delay. She had grade 2 hypertensive retinopathy.

Routine biochemistry, abdominal computed tomography, renal ultrasound and intravenous digital subtraction angiography were normal. Heart size was at the upper limit of normal on chest X-ray.

Phaeochromocytoma was excluded with a pentolinium suppression test and selective venous sampling was performed: renin levels were not elevated, and assays for catecholamines again excluded phaeochromocytoma. Arteriography was performed and demonstrated no coarctation and normal single main renal arteries, but flush aortography revealed on both sides the features of vascular neurofibromatosis in the third generation intrarenal vessels, particularly in the upper pole of the right kidney (Figure 3).

The hypertension responded to conventional treatment with atenolol and hydrochlorothiazide and amiloride, and she has now returned to Oman.

Discussion

Neurofibromatosis may be associated with vascular lesions of the aorta and its major branches, particularly the renal arteries. Hypertension in such patients may be caused by renal artery stenosis and coarctation of the aorta.

Comparing vascular neurofibromatosis with fibromuscular dysplasia, the latter affects the distal two thirds of the renal artery in 95% of cases and is commoner in middle aged females (average age 38 years); vascular neurofibromatosis causes stenosis or

Figure 3 Aortogram demonstrating irregular beaded appearance (arrowed) of the third generation intra-renal arteries.

occlusion of the renal artery at its origin in 50% of cases, is commoner in males and the average age of patients is 14.² Unlike fibromuscular dysplasia, vascular neurofibromatosis often affects the intrarenal arteries and arterioles,³ as in our two cases.

True extrinsic compression of the renal artery at its origin is rare (4% of cases of neurofibromatosis with

renovascular hypertension⁴). The commonly described lesions are those of intimal proliferation and neurofibromatotic or ganglioneuronic overgrowth in the adventitia, the media being uncommonly affected.⁵

In our first case the diagnosis of intrarenal arterial disease was made on a pathological basis following surgery to correct a stenosis of the main renal artery; in the second the diagnosis was made on aortography and it is worthy of note that these subtle changes in the intrarenal vessels were not visible on the intravenous digital subtraction angiogram.

These lesions follow an unpredictable course. Because of the intrarenal element which is frequently present and may be bilateral, surgical correction of a stenosis of the main renal artery may not permanently alleviate the hypertension and in addition, restenosis of reimplanted renal arteries has been observed.⁶ The outlook in such patients should be guarded.

The presence of normal renin levels and the therapeutic failure of captopril despite a good response to surgery in our first case raises doubt regarding the mechanism of the hypertension in this case, and the possible role of another mediator, or the effects of denervation by autotransplantation should be considered.

Acknowledgements

We acknowledge with thanks the cooperation, help and advice of Professor M. Brown, Dr S. Thiru, Dr D.S. Appleton and Dr H. Scott.

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