Case Report

Acute angulation of the left renal artery imitating renal artery stenosis in a patient with neurofibromatosis type 1

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Introduction

Neurofibromatosis type 1 (NF1, von Recklinghausen’s disease) is an autosomal dominant genetic disorder with an estimated incidence of ~1 in 4000 births [1]. Half of all cases are new mutations, of which, to date, almost 200 have been identified. The NF1 gene, which is located on the long arm of chromosome 17 in band q11.2, was identified and its protein product characterized in 1990 [2,3]. The gene is large and codes for a 2818 amino acid protein called neurofibromin, the function of which remains unknown, although a portion of the protein may be a GTPase activator involved in the regulation of Ras activity, thereby controlling cellural proliferation [4]. The diagnosis of NF1 is based largely on clinical criteria established by the National Institute of Health (NIH) Consensus Development Conference on Neurofibromatosis in 1987 (Table 1) [5].

Hypertension is frequent in NF1 and may develop at any age. In most cases, the hypertension is “essential”, but pheochromocytoma and renal artery stenosis (RAS) should always be considered as remediable causes in hypertensive NF1 patients [6].

Here, we present a 30-year-old hypertensive female patient with NF1 in whom, despite findings suggestive of RAS, obtained by non-invasive techniques, renal arteriography failed to demonstrate stenosis and the hypertension was therefore classified as essential and easily controlled by β-blockade.

Case

A 30-year-old woman was admitted to our hospital because of recently discovered hypertension. The patient had been well until 5 weeks earlier when her blood pressure was measured coincidentally and was found to be 220/110 mmHg. There was nothing of note in her past medical history; her family history was also negative, and she was on no medication. Physical examination revealed, in addition to the arterial hypertension, many café-au-lait macules (5–20 mm) and freckling on the trunk, axillae, hands and inguinal region. There was one neurofibroma on the anterior thoracic wall and one plexiform neurofibroma on the back (Figure 1). Slit lamp examination of the iris

Table 1. Diagnostic criteria for neurofibromatosis 1 (NF1)

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<th>The patient should have two or more of the following:</th>
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<tr>
<td>1. Six or more café-au-lait spots</td>
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<td>1.5 cm or larger in post-pubertal individuals</td>
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<tr>
<td>0.5 cm or larger in pre-pubertal individuals</td>
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<tr>
<td>2. Two or more neurofibromas of any type or one or</td>
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<td>more plexiform neurofibroma</td>
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<td>3. Freckling in the axilla or groin</td>
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<td>4. Optic glioma (tumour of the optic pathway)</td>
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<td>5. Two or more Lish nodules (benign iris hamartomas)</td>
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<td>6. A distinctive bony lesion</td>
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<td>Dysplasia of the sphenoid bone</td>
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<td>Dysplasia or thinning of long bone cortex</td>
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<td>7. A first degree relative with NF1.</td>
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body radioiodinated metaiodobenzylguanidine ([131I]-MIBG) scintiscan were also normal.

The renal artery Doppler ultrasonography study (Figure 2) revealed high systolic velocity near the origin of the left renal artery, compatible with haemodynamically significant stenosis, but no abnormalities in the intrarenal segmental branches of the vessel were found. The 99mTc-diethylenetriaminepentaacetic acid renal scintiscan (99mTc-DTPA) after captopril administration (Figure 3) also disclosed alterations in renal function on the left, compatible with haemodynamically significant RAS. Magnetic resonance angiography, employing a 2D phase contrast technique without i.v. administration of contrast medium, suggested a stenosis at the origin of the left renal artery (Figure 4), and revealed a second, small left renal artery 1 cm below the main vessel. However, the abdominal aortogram with selective renal artery catheterization failed to demonstrate any stenosis (Figure 5). The patient was given a β-blocker with appropriate control of her blood pressure.

Discussion

NF1 is a genetic disease with an extremely wide range of clinical manifestations. Cutaneous features, including café-au-lait spots and intertriginous freckling, occur in >90% of patients. Neurofibromas may affect almost any organ in the body. Hypertension is frequent in
Acute angulation of the left renal artery in a patient with NF1

The association of vascular lesions and neurofibromatosis occurs most frequently in the abdominal aorta and its branches, especially the renal arteries. There are two basic categories of vascular lesions associated with neurofibromatosis [9]. The first involves larger vessels such as the aorta and the proximal portions of the renal arteries, which are surrounded by fibromatous tissue. The second type affects the vessel wall itself and may involve all its layers. These changes are felt to reflect a mesodermal dysplasia, which can occur in multiple arteries and may also involve small intrarenal branches, making repair difficult.

The life expectancy of patients with NF1 is reduced by at least 15 years overall [10]. Malignancy and hypertension are important contributors to the increased mortality seen in adult NF1 patients. Consequently, it is important to be aggressive diagnostically in order to make a timely diagnosis of malignancies or of interventionallly remediable causes of hypertension.

In our patient, the renal artery Doppler ultrasound, magnetic resonance angiography and 99mTc-DTPA renal scintiscan were interpreted as indicative of left RAS. However, the conventional aortogram with selective renal angiography disclosed no stenosis, but only origination of the left renal artery from the aorta at an unusually sharp angle.

This anatomical variation probably explains the false-positive results of both the magnetic angiography and the Doppler sonography, techniques which both rely on high blood flow velocities for identification of haemodynamically significant RAS. Left renal artery blood flow velocities were probably falsely overestimated by the unusually oblique direction of our patient’s left renal artery. The renal scintigram result on the other hand, indicating angiotensin dependence of left renal perfusion, may have resulted from intra-renal vessel (arteriolar) lesions, which were angiographically non-demonstrable, and interventionally non-removable.

Contrast enhanced 3D magnetic resonance angiography is not liable to flow-dependent artefacts and may, therefore, be the non-invasive technique of choice; however, it requires specific software and i.v. administration of contrast media [11]. However, confirmation of RAS suggested by non-contrast enhanced magnetic resonance angiography or Doppler ultrasound continues to require conventional or digital arteriography.

NF1 and may develop at any age. As in our patient, hypertension is usually essential, but remediable causes should be excluded. In patients over the age of 18 years, pheochromocytoma is the predominant remediable cause, while in patients below the age of 18 years, RAS seems to predominate [8].

References

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