

Neurofibromatosis with Bilateral Renal Artery Stenosis and End Stage Renal Disease

Case Report

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مرض الورام العصبي الليفي مع تضيق الشرايين الكلوية الثابتة وفشل كلوي بالمرحلة النهائية تقرير حالة

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الملخص: الورام العصبي الليفي - النوع الأول هو مرض وراثي ذو صفة وراثية سائدة . وهو عبارة عن متلازمة عصبية جلدية تصيب مختلف أعضاء أو أجهزة الجسم بصفة أولية أو ثانوية . ومن ضمنها الجهاز القلبي الوعائي . وأكثر الأوعية الدموية تأثراً بالمرض هي الشرايين الكلوية التي تصاب بالتضيق مما يؤدي إلى ارتفاع ضغط الدم. هنا نعرض تقريراً وصفياً بحالة مريض في أواسط العمر راجع مستشفى جامعة السلطان قابوس وقد أصيب بفشل كلوي بالمرحلة النهائية مصحوباً بارتفاع شديد في ضغط الدم ناتج عن تضيق الشرايين الكلويين جراء الإصابة بمرض الورام العصبي الليفي.

مفتاح الكلمات: مرض الورام العصبي الليفي . تضيق الشريان الكلوي . فشل كلوي بالمرحلة النهائية . ارتفاع ضغط الدم كلوي المنشأ . غسيل كلوي . تقرير حالة . عمان .

ABSTRACT: Neurofibromatosis type 1 (NF-1) is an autosomal dominant, hereditary, neurocutaneous syndrome that may, primarily or secondarily, affect different organs or systems of the body including the cardiovascular system. The most common vascular abnormality in patients with NF-1 is renal artery stenosis. Here we report the case of a middle-aged gentleman who presented at Sultan Qaboos University Hospital, Oman, with end stage renal disease and severe hypertension and was diagnosed to have NF-1 with bilateral renal artery stenosis. He was started on renal replacement therapy.

Keywords: Neurofibromatosis; Renal artery stenosis; End stage renal disease; Renal hypertension; Haemodialysis; Case report; Oman.

TYPE 1 NEUROFIBROMATOSIS (NF-1) IS A common genetic disorder, with variable clinical manifestations, which affects at least one million persons throughout the world. Although rare, vascular abnormalities are a well-recognised manifestation of neurofibromatosis and may lead to renal artery stenosis and renovascular hypertension. Here, we present the case of a young Omani man who presented with end stage renal disease (ESRD) and severe hypertension, and was diagnosed to have NF-1 with bilateral renal artery stenosis.

Case Report

A 37 years old Omani man presented at Sultan Qaboos University Hospital, Oman, with a

headache of two years duration and was found to be severely hypertensive. Upon presentation, his blood pressure was 190/105 mmHg. His past medical history was significant for decreasing hearing in the left ear since early childhood. His family history was significant for neurofibromatosis in one son.

The patient was evaluated for the possibility of neurofibromatosis. He was noted to have decreased hearing in the left ear due to mastoid sinus disease and fundoscopy revealed Lisch nodules. Clinically, the patient had multiple café au lait spots and a neurofibroma in the cervical region. Laboratory investigations revealed: creatinine 1387umol/L; urea 71 mmol/L; bicarbonate 7mmol/L and potassium 5.4 mmol/L. The urine dipstick was positive for proteins (+2) and trace red blood cells (RBC). Urine microscopy showed few RBCs and numerous

granular casts. Haemoglobin was 10.1 g/dl; platelets 204×10^9 ; serum catecholamines 1 pmol/l; serum calcium 1.89 mmol/l and serum phosphate was 3.81mmol/l. Tests for cytoplasmic antibodies (ANCA), anti-nuclear antibodies (ANA), hepatitis B, hepatitis C and HIV 1&2 were negative.

An ultrasound of the abdomen demonstrated that both kidneys were small in size with significantly increased cortical echogenicity. The left kidney measured 8.1 cm in length and the right kidney 7.8 cm. A renal magnetic resonance angiography (MRA) showed severe proximal bilateral renal artery stenosis [Figure 1]. Magnetic resonance imaging (MRI) of the head showed chronic otitis media with mastoiditis and an intercostal neurofibroma in the cervical area.

The patient was started on haemodialysis three times per week with a satisfactory outcome. His blood pressure was controlled on atenolol. An arteiovenous fistula was created for long term renal replacement therapy. He had no potential donor for a kidney transplant.

Discussion

Neurofibromatosis is an autosomal dominant neurocutaneous disorder with an incidence of approximately 1 in 3,000 individuals.¹ Approximately half of the cases are familial and the remainder are due to new mutations.² The diagnostic criteria developed by the National Institutes of Health are based upon the presence of specific clinical features, at least two of which must be present to make a diagnosis of NF-1:¹

1. Six or more café au lait macules >5 mm in diameter in prepubertal and >15 mm in diameter in postpubertal individuals.
2. Two or more neurofibromas of any type or one plexiform neurofibroma.
3. Freckling in the axillary or inguinal regions.
4. Optic glioma.
5. Two or more Lisch nodules (iris hamartomas)
6. A distinctive bony lesion such as sphenoid dysplasia or thinning of the long bone cortex with or without pseudoarthrosis.
7. A first-degree relative with NF-1 based upon the above criteria.

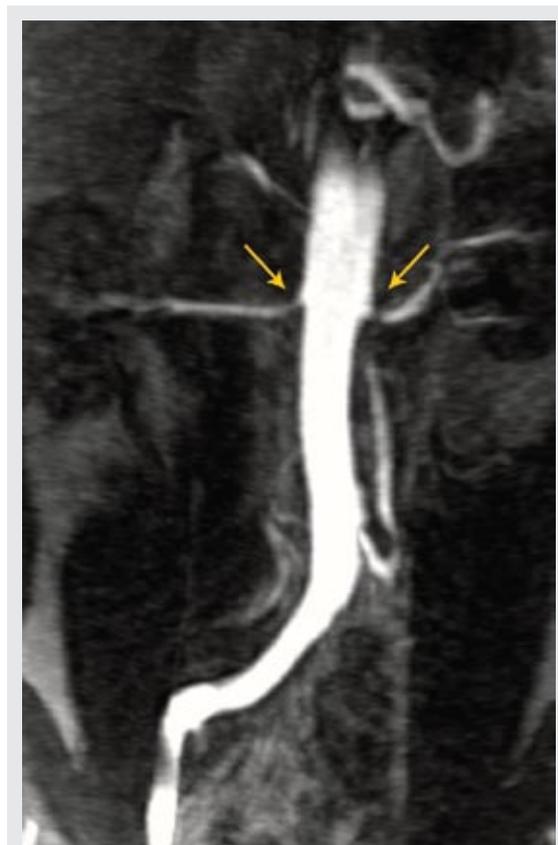


Figure 1: Minimum Intensity Projection (MIP) of magnetic resonance angiography (MRA) of the renal arteries shows severe stenosis of the proximal segments of both renal arteries (arrows).

The cardinal features of NF-1 in this patient were the presence of Lisch nodules and a positive family history. This patient illustrates the complete penetrance of the affected gene. The likelihood is that individuals carrying the mutation will be affected over several generations, but with a variable expression of the disease.³

Hypertension is a frequent finding in adults with NF-1 and may develop during childhood. It is found in most cases, but vascular lesions producing renovascular hypertension are more frequent in NF-1 patients.⁴ Renovascular lesions can be detected in patients who are still normotensive; the frequency with which such patients will develop hypertension is not known. Coarctation of the aorta is a known cause of hypertension that also tends to occur in NF-1. A much less common cause of hypertension in NF-1 is pheochromocytoma, which has been clinically identified in 0.1 to 5.7% of patients. The mean age at diagnosis was 42 years.⁵

Our patient had hypertension upon presentation and was found to have bilateral proximal renal artery

stenosis. Serum catecholamine levels were normal hence pheochromocytoma was ruled out as a cause of secondary hypertension.

Most patients with NF-I vascular abnormalities are asymptomatic, but have involvement of multiple vessels.⁶ The prevalence of vascular lesions is not well known, however, large clinical series estimate them to be around 0.4% to 6.4%.⁶ Symptoms usually occur in childhood or early adulthood. The renal artery is the most frequent site of involvement with a prevalence of 41% of all vascular abnormalities, of which 68% are unilateral. In addition, these lesions are more stenotic than aneurysmal.⁷ Renovascular hypertension is the most common presentation of these vascular abnormalities.⁸ Abdominal aortic coarctation, internal carotid artery aneurysms, and cervical vertebral arteriovenous malformations are other common manifestations.⁸

End stage renal disease (ESRD) has been reported in very few individual case series in the literature due to chronic ischaemia of the kidneys as a result of renal vascular abnormalities. This patient had ESRD which was due to bilateral renal artery stenosis and secondary hypertension. His ESRD was managed with renal replacement therapy as no suitable donor was found. His hypertension was managed with atenolol with good response.

Percutaneous transluminal angioplasty (PTA) had a limited role for this patient as the blood pressure was well controlled with anti-hypertensive therapy. Renal failure would have not improved with PTA as both kidneys were small and indicated chronic renal insult. Moreover, the success due to the ostial localisation of renal arterial stenosis (RAS) and the tough fibrotic tissue involved is often refractory to dilatation.^{9, 10} Nephrectomy would have been a probable choice if blood pressure were difficult to manage medically.

Conclusion

In summary, neurofibromatosis is a disorder usually associated with unilateral RAS. We believe that this is the first case report of this condition to present

as ESRD. All young patients (< 30 year) with hypertension should be clinically screened very early for secondary causes of hypertension including neurofibromatosis so that renal revascularization can be offered before permanent end organ damage has occurred as in this patient.

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