Neurofibromatosis with Renovascular Hypertension

A CASE REPORT

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SUMMARY

A 13-year-old Black patient presented with neurofibromatosis complicated by hypertension. Repeated normal vanillylmandelic acid estimations seemed to exclude a phaeochromocytoma. A transfemoral aortogram showed a double left renal artery, one branch narrowed with a post-stenotic dilatation, and the other dilated. The ratio of left to right renal vein renin values was 1,75. Reconstructive surgery was not possible, and a nephrectomy was done. The blood pressure decreased during the 3-week post-operative period before the patient was discharged.

A short review of the literature is presented.

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Neurofibromatosis (von Recklinghausen's disease) is a Mendelian-dominant inherited disease typified by areas of increased skin pigmentation (café-au-lait spots) and multiple neurofibromata. The majority of these tumours become symptomatic if they are very large, or are present in unusual positions (e.g. acoustic neuroma). Other histopathological types of tumour, e.g. meningioma or glioma, are more common in patients with neurofibromatosis than in the general population.

The associated anomalies of this disease are protean. Skeletal abnormalities include congenital vertebral changes, local gigantism of an extremity and subperiosteal bone cysts. These changes may eventually lead to scoliosis, common in children with this disease, and it can be considered as one of the neurogenic causes of kyphoscoliosis.

Hydrocephalus may result from stenosis of the aqueduct of Sylvius, and mental retardation is common in familial neurofibromatosis. Hypospadias, glaucoma and elephantiasis have been described.

The majority of patients with neurofibromatosis seek advice because of the cosmetic effects of the tumours or because of a neurological complication.

A small minority of patients may also have hypertension. There is a distinct association between neurofibromatosis and phaeochromocytoma, but in recent years vascular neurofibromatosis, including coarctation of the abdominal aorta, and lesions of the renal arteries have been documented.[1] The renal artery lesions, chiefly aneurysmal dilatation, or stenosis with post-stenotic dilatation, may be associated with hypertension. Renal artery stenosis and aneurysm, and coarctation of the abdominal aorta, are rare childhood conditions, and are found only in neurofibromatosis.[2] We could find only 20 well-documented cases of renal artery neurofibromatosis with stenoses and associated hypertension in the literature.

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CASE REPORT

A 13-year-old Black patient was admitted to hospital because of an attack of epilepsy. There was no family history of epilepsy and he had never been ill before. There were multiple small tumours, which had the appearance of neurofibromata, present on his chest, abdominal wall and back, in addition to many café-au-lait spots of varying sizes. His blood pressure was 150/100 mmHg in both arms, and 180/120 mmHg in the legs. There was marked spasm of the retinal arteries. The left side of the chest was more prominent than the right owing to abnormalities of the ribs, and slight kyphoscoliosis was noted. There was no abdominal visceromegaly and no murmur was audible over the renal arteries. The central nervous system showed no abnormality and the remainder of the clinical examination was within normal limits. The electrocardiogram showed left axis deviation with left ventricular hypertrophy.

Histological examination of one of the tumours confirmed the diagnosis of neurofibromatosis.

The chest X-ray film showed the so-called 'twisted ribbon' appearance typical of neurofibromatosis of the ribs (Fig. 1). X-ray films of the skull and thighs were normal.

The serum electrolytes, uric acid, creatinine and urea values were normal, but the creatinine clearance was decreased to between 52 and 65 ml/min. A hypertensive intravenous pyelogram was normal. Repeated 24-hour urine estimations for vanillylmandelic acid varied from 0,1 to 0,3 mg/day.

An isotope renogram revealed reduced blood flow and reduced isotope concentration in the left kidney. The right kidney appeared to be normal. These findings suggested a malfunctioning left kidney, and a transfemoral aortogram and selective renal arteriograms were done. These showed the left kidney to be supplied by two renal arteries. The one was stenosed with a post-

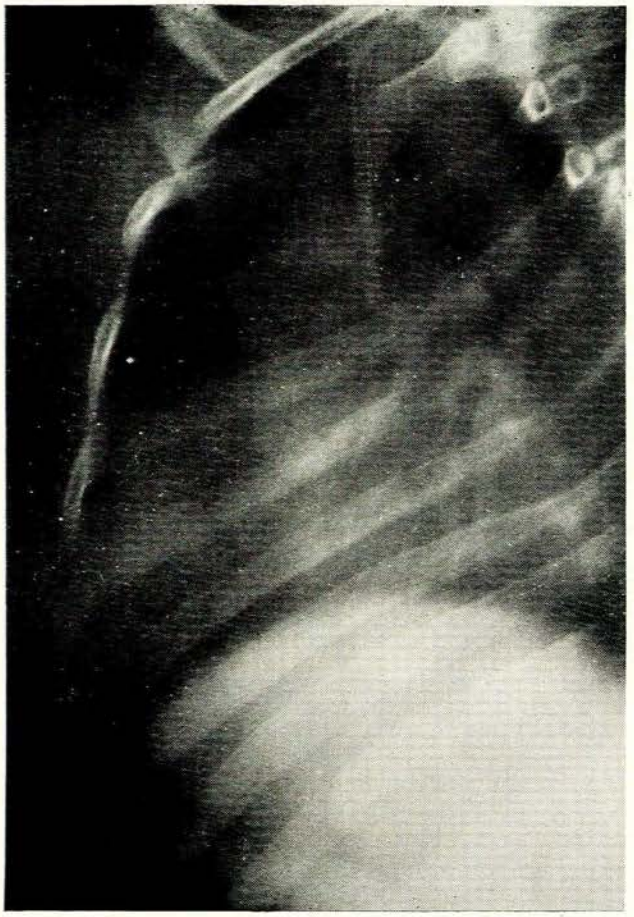

Fig. 1. Chest X-ray film showing the typical 'twisted ribbon' appearance of the ribs.

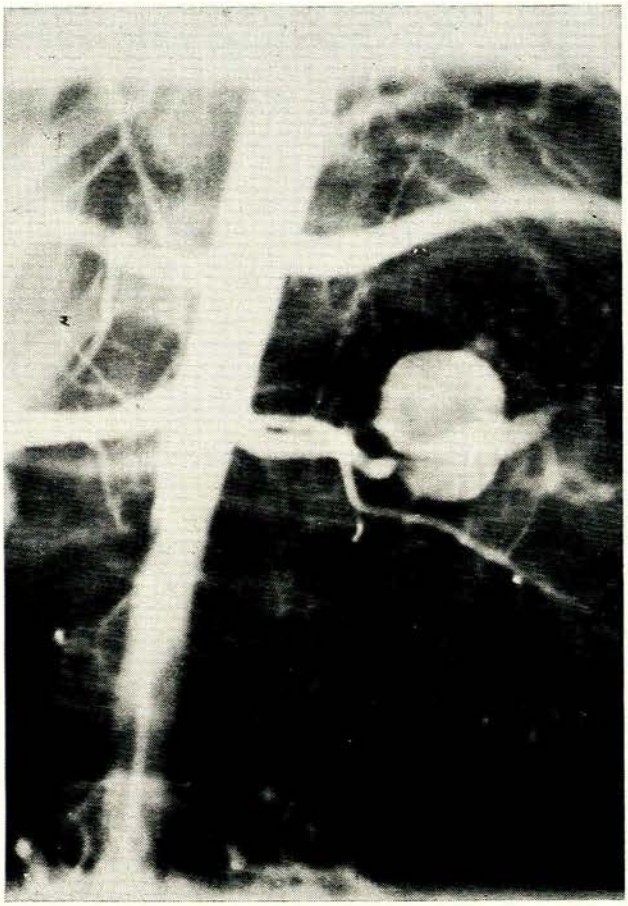

Fig. 2. Renal arteriogram showing the lesions of both left renal arteries (see text).

stenotic dilatation, and the other appeared to be aneurysmally dilated (Fig. 2). The right renal artery and the smaller intrarenal branches seemed to be normal.

The values of the plasma renin determinations done at the time of the arteriogram are given in Table I. There was a high circulating renin concentration, possibly due to excessive secretion from both kidneys. The relationship of left to right renal vein concentrations was 1,75, which suggested that the left-sided stenosis was probably contributing to the hypertension, and reconstructive surgery was undertaken.

TABLE I. PLASMA RENIN VALUES IN OUR PATIENTS*

Peripheral vein	592
Inferior vena cava — above renal veins	726
Left renal vein (LRV)	919
Right renal vein (RRV)	524
Arterial specimen	654
LRV/RRV ratio	1,75

* Normal for our laboratory 0-250.

The left kidney was removed and prepared for autotransplantation. The main left renal artery split into anterior and posterior divisions. The anterior branch was almost totally occluded by a stenotic lesion, with a large distal aneurysm. The posterior artery was also stenosed, with a post-stenotic dilatation. It was technically impossible to repair the stenoses, and the nephrectomy was completed.

Microscopic examination showed the stenoses to be due to neurofibromatous thickening of the intima (Fig. 3). A number of axons were demonstrated in this tissue by using Palmgren's silver impregnation method. The media was thin and atrophic and the adventitia thickened, owing to mild fibrosis. There was no infiltration by lymphocytes or neutrophils. The interlobular, arcuate and intralobular arteries, as well as the rest of the kidney, appeared normal.

The immediate postoperative blood pressure remained at 160/110 mmHg, but a week later it had already dropped to 130/90 mmHg and was 120/85 mmHg when the patient was discharged from hospital 3 weeks after the operation. He was receiving no antihypertensive treatment at that stage.

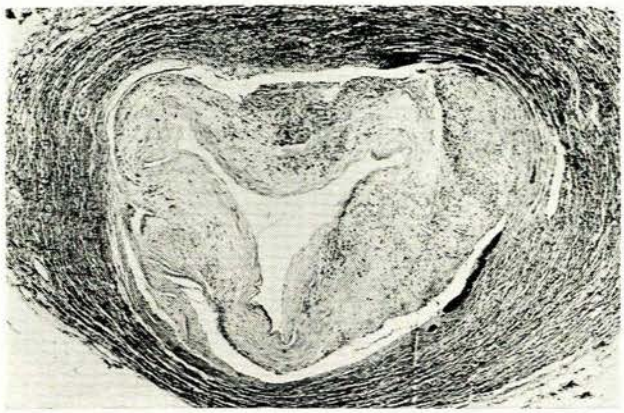

Fig. 3. Photomicrograph (× 40) showing neurofibromatous intimal thickening of the renal artery.

DISCUSSION

Arterial lesions complicating neurofibromatosis have been occasionally reported since 1905, and in the early literature these lesions were thought to be identical with those of periarteritis nodosum.[3] However, Reubi (as quoted by Halpern and Currarino[3]) concluded that the vascular lesions of neurofibromatosis were a separate entity, and that the specific histological appearance varied with the size of the vessels: (*i*) arterioles of 50 - 400 μm in diameter showed layers of endothelial cell proliferation, an atrophic media and elastic layer, and normal adventitia; (*ii*) larger arteries (5 - 10 mm in diameter) developed a fibrohyaline thickening of the intima, with disorganisation of the smooth muscle predisposing to the development of small aneurysms; and (*iii*) arteries of 100 - 700 μm may develop nodules in the adventitia around the vasa vasorum.

The first large series (10 cases) of renovascular hypertension with neurofibromatosis was reviewed in 1965.[3] There have subsequently been sporadic reports of a further 10 cases.[4]

Of the 20 cases presented, 18 were younger than 17 years at the time of diagnosis. Seventeen were operated on in an attempt to control the blood pressure. Local repair or bypass of the renal artery lesions was done in 9, and nephrectomy in 7 cases (the nature of the operation in 1 case is not mentioned). The blood pressure returned to normal in 8 cases seen in long-term follow-up, and remained elevated in 6. No follow-up was reported in the rest.

Reconstructive surgery is often unsuccessful and many of these young patients are subjected to nephrectomy. Even so, a large percentage of patients remain hypertensive after both nephrectomy and reconstructive procedures.

These disappointing results suggest the possibility of lesions of the smaller vessels in the contralateral kidney.[5-7] It may be possible to predict the response to surgery by differential renin determinations, but very few such investigations in neurofibromatosis have been reported. In one case[5] a peripheral venous renin was normal; in another[7] the peripheral venous renin (measured in the inferior vena cava) was well above normal, and the ratio of the left to right renal vein was 1,28. The blood pressure 2 months after operation was normal in this case, but the patient was receiving low-dose antihypertensive drugs.

In our patient the ratio of left to right renal vein renin was 1,75, but peripheral renin was also grossly elevated, possibly indicating that the contralateral kidney was also secreting an excessive amount of renin.

A cautious approach to surgery in these cases is recommended[9] because reconstructive operations are not always possible and nephrectomy has to be carried out, and because the blood pressure often remains elevated, even after nephrectomy. The plasma renin value and ratio of left to right renal vein renin may assist in deciding which cases will respond to nephrectomy.

Renovascular hypertension must be considered when assessing a patient with neurofibromatosis complicated by hypertension.

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