HYPERTENSION AND UNILATERAL RENAL DISEASE TREATED BY NEPHRECTOMY

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At the present time most patients with hypertension can only be offered mitigation of their disease and alleviation of their symptoms. Cure is possible only in certain well-defined syndromes such as phæochromocytoma, primary hyperaldosteronism, coarctation of the aorta, and unilateral renal disease. The work relating to this last cause of hypertension has recently been reviewed by Smith (1956) who analysed 575 cases, reported from 1937 to 1956, in which nephrectomy was carried out for proven or suspected unilateral renal disease with associated hypertension. Of these 575 cases, 149 were "cured" by nephrectomy, in that their blood pressure fell to 140/90 or less for a period of at least a year after operation. The commonest lesion found at nephrectomy was pyelonephritis and, less commonly, hydronephrosis, atrophic kidney, and arterial occlusion.

In this paper we describe the effect of nephrectomy in three further cases.

Case 1. A married woman of 48 complained of headaches and vertigo for several months. Apart from menopausal symptoms and a "feeling of being run down", she was otherwise well.

Physical examination was normal, except for a blood pressure of 210/110 mm. Hg at rest. Hypertension had originally been discovered by her family doctor five weeks previously and repeated examinations showed the pressure to vary between 260/120 and 210/110.

Tests of urine function showed a blood urea of 45 mg. per 100 ml. and van Slyke urea clearance of 85 per cent of normal. Urine dilution and concentration tests gave a specific gravity range of 1001 to 1017.

X-ray studies of the urinary tract revealed no secretion on the left side on intravenous pyelography. Retrograde pyelography showed a left-sided hydronephrosis (Fig. 2).

During a sodium amytal sedation test the blood pressure fell from an initial level of 220/110 to 120/60, whilst the patient was asleep. Examination of the fundi showed grade II hypertensive retinopathy.

In view of the labile hypertension and of the non-functioning hydronephrotic kidney, a left nephrectomy was carried out. Convalescence was straightforward.

The kidney was small and shrunken and weighed 50 g. There was severe hydronephrosis, affecting the pelvis and major calyces, while the renal parenchyma was distorted and showed increased fibrosis. On microscopic examination, the appearances were those of hydronephrosis with chronic pyelonephritis.

Six months later, her blood pressure was 170/100 and she said she felt well except for occasional headaches. She was re-examined, one, two, three, and five years after operation. On each occasion she reported that she was well and free from symptoms. Her blood pressure remained steadily at 160–170 systolic and 85 to 90 diastolic (Fig. 1).

Case 2. A boy, aged 10 years, was admitted on 1/5/55 in a stuporose condition. He had been treated at the age of 4 years for urinary tract infection and intravenous pyelography at that time had disclosed dilatation of the left renal pelvis. Unfortunately he had not attended the follow-up clinic, in spite of the fact that he developed enuresis and became increasingly tired during the next six years.

Two days before admission he vomited and became drowsy and the next day he complained of a headache and became disorientated. Shortly after admission he had generalized epileptiform convulsions. His blood

FIG. 1.—Serial blood pressure recordings, before and after nephrectomy, in Case 1.

FIG. 2.—Unilateral hydronephrosis in Case 1, a woman of 48, with severe hypertension.

FIG. 3.—Intravenous pyelogram in Case 2, a boy, aged 10 years, showing left-sided hydronephrosis with poor renal function.

pressure was found to be 240/130, retinal hæmorrhages and papillœdema were present, and a diagnosis of hypertensive encephalopathy was made. Treatment with intramuscular phenobarbitone and magnesium sulphate and lumbar puncture resulted in rapid improvement and on the next day he was rational and cooperative. Examination showed him to be a thin boy, weighing 65 pounds, and 55 inches tall. His blood pressure was 210/160. The following investigations were carried out.

Blood: Hæmoglobin 13.5 g. per 100 ml.; white cell count 7000 per c.mm. Erythrocyte sedimentation rate (Westergren) 17 mm. in the first hour. Blood urea 40 mg. per 100 ml. *Urine:* Specific gravity fixed at 1012–1013. Albumin and large numbers of pus cells present. *Proteus vulgaris* cultured. *Chest X-ray:* Normal. *Electrocardiogram:* Normal. *Intravenous pyelography:* Both kidneys functioning. Right normal; dilatation of calyces on the left (Fig. 3). *Urea clearance:* Maximum clearance was 61 per cent of average normal (corrected for surface area).

His condition improved further on treatment with phenobarbitone and chloramphenicol, but the blood pressure averaged 200/140. Three weeks after admission his blood pressure rose to 255/190, he became drowsy and restless, and treatment with hexamethonium was started. In spite of this the diastolic pressure remained high, fluctuating between 140 and 170, and it was, therefore, decided to remove his left kidney. Nephrectomy was carried out on 27/5/55 and the kidney was found to be small and fibrotic, showing the changes of chronic pyelonephritis on microscopy.

After operation the blood pressure remained about 200/160 and, on the fourth post-operative day, further convulsions occurred and he developed gross papillœdema and retinal exudates. Since hexamethonium had not proved very effective, treatment was instituted with pentolinium, increasing the dose to 20 mg. six-hourly, and later rauwiloid 2 mg. 12-hourly, was added. On this regime the blood pressure became stabilized at about 125/90 and his general health steadily improved. He was discharged from hospital three months after his original admission, at which time his urine was free from pus cells, the blood urea was 30 mg. per 100 ml., and urea clearance tests showed that function was essentially unchanged.

His behaviour in the ward had been noted to be abnormal, with frequent temper tantrums and immoderate laughter. At first this was attributed to cerebral damage sustained during the fits, but enquiry showed that his I.Q. at the age of 7 years had been assessed at 85, and that his brother had an I.Q. of 70 and was at a special school. The condition may therefore be hereditary.

He attended hospital as an out-patient for the next two years, during which period his general health was good. The systolic blood pressure remained at about 125 to 130 and the diastolic at 90 to 100, the recordings being made after the patient had been lying quietly for 10 minutes. He was re-admitted in June, 1957, for assessment. His blood pressure, during six weeks observation in hospital, averaged about 110/70, the systolic pressure ranging from 130 to 100 and the diastolic from 90 to 50. Pentolinium was gradually withdrawn without significant alteration in the blood pressure. His urine was free from albumin and sterile on culture, and the blood urea was 36 mg. per 100 ml. The blood pressure remained at about 125/85 during the next six months on treatment with rauwiloid alone, and this drug was therefore also gradually withdrawn. When last seen at the age of 13 years, he was in excellent health without treatment, his weight being 94 pounds and his height 61½ inches. His blood pressure was 125/90, his heart and optic fundi were normal on examination, and his urine contained no albumin, the pH being 5.5 and the specific gravity 1014. The following normal biochemical results were obtained: blood urea 30 mg. per 100 ml.; serum cholesterol 172 mg. per 100 ml.; serum albumin 4.1 g. per 100 ml.; serum globulin 2.1 g. per 100 ml.; plasma creatinine 0.93 mg. per 100 ml. He is thus in good health and has a normal blood pressure, without treatment, three years after nephrectomy (Fig. 4).

Case 3. A 36-year-old man attended the ophthalmic department complaining of occasional blurring of vision, headache, and giddiness. Eight years previously he had had an episode of backache and some vomiting, but otherwise there was nothing significant in his past history. His parents were alive and well. He was a well-nourished, healthy-looking man. His blood pressure was 205/130. The fundi showed bilateral early papillœdema and several hæmorrhages and exudates. Otherwise physical examination was negative. The following examinations were made.

Blood: Hb. 15 g. per 100 ml. White cell count 7600 per c.mm. E.S.R. 30 mm. in the first hour (Westergren). Urea 24 mg. per 100 ml. Urea clearance 135 per cent average normal. *Urine:* Mid-stream sample—culture negative; no abnormality in centrifuged deposit. Random specific gravity 1025. No albumin. *Chest X-ray:* Normal. *Electrocardiogram:* Left ventricular hypertrophy (Fig. 5). *Sedation test* (9 grains sodium amylal): Blood pressure fell from initial reading of 180/135 to 140/105. *Phentolamine test* (5 mg. I.V.): Blood pressure fell from 175/135 to 140/100 in the first minute, thereafter rising to 150/110

FIG. 4.—Serial blood pressure recordings in Case 2, before and after left nephrectomy.

FIG. 5.—Electrocardiograms in Case 3, before and after left nephrectomy for severe hypertension with occlusion of the left renal artery. Hypertension cured by nephrectomy, 12/3/57.

and remaining at this level for the next 15 minutes. 24-hour output of catechol amines: Nor-adrenaline 26 μ g. Adrenaline 3.7 μ g. (These values are within normal range.) Intravenous pyelography. Right kidney and ureter normal. No function on left side. Retrograde pyelography. Right kidney normal. Left kidney shows some dilatation of pelvis, without dilatation of the calyces (Fig. 6). Aortography (Fig. 7): The left renal artery is occluded about 1 cm. from the aorta. The right renal artery is normal.

FIG. 6.—Retrograde pyelography in Case 3, showing a left-sided hydronephrosis.

FIG. 7.—Aortography in Case 3, showing occlusion of the left renal artery 1 cm. from the aorta.

FIG. 8.—Left renal artery of Case 3, showing occlusion of the lumen with recent thrombus. The thrombus proved histologically to lie in the media and to be in the nature of a dissecting aneurysm.

FIG. 9.—Photograph of kidney removed in Case 3. The upper pole of the kidney is white and avascular.

A diagnosis of early malignant hypertension with unilateral renal arterial occlusion and hydronephrosis was made and left nephrectomy was performed on 12/3/57. It was noted that the renal artery was occluded by recent thrombus (Fig. 8).

The pathological report by Dr. H. D. Attwood on the specimen (Fig. 9) was as follows.

"Left Kidney. The specimen consisted of a hydronephrotic kidney ($12 \times 6 \times 3$ cm.). The dilated pelvis (150 ml.) was interposed between the renal vein anteriorly and the renal artery posteriorly. The mucosa of the pelvis was granular and focally injected. The renal artery and all its major branches showed the appearances of a dissecting aneurysm. Microscopic examination showed glomerular hyalinization, interstitial fibrosis, and tubular atrophy in keeping with a hydronephrosis. The pelvis was lined by a non-specific inflammatory granulation tissue, with an unusual proportion of eosinophils. The renal arteries showed intimal proliferation, and in the main renal trunk and its major branches there was dissection of blood in the media, immediately internal to the external elastic lamina. The intimal entry for such blood was not seen in the representative sections examined. The elastic laminae were intact and there was no evidence of cystic medial necrosis. The blood within the media showed little evidence of organization and there was merely a focal adventitial inflammatory reaction with aggregations of polymorphs in several places. The appearances were those of a hydronephrosis with a pyelitis and dissecting aneurysm of the renal artery and its main branch. The aetiology of the dissecting aneurysm was obscure. The intimal lesion permitting such a dissection was not in the specimen."

Post-operatively the blood pressure fell to a normal level (Fig. 10). He was rather pale and nauseated on 13/3/57, when his blood pressure was at its lowest (100/80), but otherwise he had a satisfactory convalescence. The retinopathy regressed quickly and the electrocardiogram reverted to normal (Fig. 5).

He was seen regularly after operation and his blood pressure varied between 120/80 and 120/90. He now enjoys normal health and his blood pressure, one year after nephrectomy, was 120/75.

FIG. 10.—Serial blood pressure recordings in Case 3, before and after nephrectomy.

DISCUSSION

There is still some empiricism in the treatment of unilateral renal hypertension, and good judgment and understanding of the natural history of renal disease are required in selection of cases for nephrectomy. Where there is no obvious operative hazard and the diseased kidney is non-functioning, as in our Cases 1 and 3, decision is usually easy. In other patients, as in Case 2, where the diseased kidney has some function, it is important to balance the loss of functioning renal tissue against the likelihood of lowering blood pressure and thereby preventing or possibly reversing hypertensive disease in the good kidney.

It is in this group that split function studies may supplement intravenous and retrograde pyelography and renal angiography, in determining the likelihood of successful reduction of blood pressure by nephrectomy. An ischaemic kidney, that is maintaining hypertension, usually secretes urine less in volume and with lower sodium concentration than that obtained from the healthy kidney (Howard *et al.*, 1956). In this regard, investigation could be regarded as incomplete in Case 2, though the severity of his symptoms necessitated urgent, even if empiric, treatment. Moreover the clinical pattern of severe hypertension, with a diastolic pressure of over 130 mm. Hg, convulsions, and severe retinopathy with papilloedema, fulfilled the diagnostic criteria required by Perera and Haelig (1952) for expectation of successful nephrectomy.

The rigid criteria of cure of Homer Smith (1956)—“established pre-operative hypertension and a post-operative reduction to 140/90, or below, for at least one year”—were not satisfied in Cases 1 and 2. In the case of the first patient, a fall of blood pressure from 220/110 pre-operatively to 160–170/85–90 post-operatively, in a 48-year-old woman, could reasonably be expected to give improved health and an increase in expected life span. Moreover, it has been argued by Poutasse and Dustan (1957) that Homer Smith's rigid criteria could well be modified, so that a fall of blood pressure post-operatively to within the normal range for age and sex (Master *et al.*, 1950) is adequate to qualify for cure. We agree with this modification of the criteria and therefore suggest that our first patient was cured by nephrectomy of moderate hypertension.

The second patient is the most difficult one to assess. He was rescued from a desperate state of malignant hypertension by hypotensive drugs, but, after a period of two years' treatment, these drugs were gradually withdrawn and a year later he was in good health with a blood pressure of 125/90. We think it likely that this patient failed to have an immediate response to nephrectomy (in striking contrast to Case 3), because the remaining kidney also had pyelonephritis or, more likely, severe hypertensive changes. It is well known that such hypertensive changes, short of malignant nephrosclerosis, can regress, after the ischaemic kidney has been removed. This may well have occurred in our case. It is interesting that it was imperative to continue hypotensive agents in the post-operative period, because of continued hypertension and convulsions. These were administered for two years subsequently, though they might have been withdrawn more rapidly. At any rate, the ultimate clinical state was satisfactory. The blood pressure reading of 125/90 three years after nephrectomy would qualify for cure, according to the criteria of Smith, but it is slightly high for a child of 13 years and we should be cautious about his prognosis.

The third patient had combined lesions of hydronephrosis and dissecting aneurysm of the renal artery, either of which could lead to renal ischaemia and resulting hypertension, although we strongly favour the arterial lesion. Renal arterial occlusion, as a cause of hypertension, has come into prominence recently. Margolin *et al.* (1957) have collected 15 case reports, including one of their own, in which hypertension due to renal arterial occlusion was cured by nephrectomy or vascular surgery, and Poutasse (1956, 1957) has written extensively on the subject. More recently, Gellman (1958) has reviewed 26 case reports and added one of his own. Twenty-four of these 27 were cured by nephrectomy, or thrombo-endarterectomy. In only one of these patients, the case of Gilfillan *et al.* (1956), was the arterial lesion a dissecting aneurysm, as in our patient. The value of aortography in the diagnosis of arterial occlusion is illustrated in our case and is emphasized by Poutasse and Dustan (1957) and Gellman (1958).

SUMMARY

Three cases of severe hypertension associated with unilateral renal disease are described. Two had hydronephrosis and pyelonephritis and one had hydronephrosis and renal arterial occlusion due to dissecting aneurysm. Nephrectomy was carried out in each case and the follow-up periods are 5, 3, and 1 years respectively. Criteria of cure are discussed. Cure is claimed for the patient with arterial occlusion, and, with reservations, cure could also be claimed for the other two patients. The value of aortography in demonstrating renal arterial occlusion is illustrated.

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