Case reports

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Renal artery stenosis with severe hypertension *A rare case with detailed assessment of renin-angiotensin system before and after development of lesion*

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SUMMARY The rare opportunity arose to assess in detail the renin-angiotensin system before and after the development of a renal artery stenosis with severe hypertension. Peripheral plasma concentrations of renin, angiotensin II, and aldosterone were known to be normal before the development of renal artery stenosis, and there were no lateralising features on renal vein sampling. Acute hypertension associated with very high peripheral plasma concentrations of renin and angiotensin II, and with pronounced lateralisation on renal vein sampling followed the development of acute unilateral renal artery stenosis. These measurements all returned to normal after nephrectomy, conforming with the pattern of changes previously established only in experimental animals.

Unilateral renal artery constriction is a classical means of inducing experimental hypertension (Goldblatt *et al.*, 1934), and renal artery stenosis is a well recognised, potentially correctable cause of clinical hypertension (Foster *et al.*, 1975). After constricting a renal artery in animals, blood pressure rises within hours and this can be accounted for quantitatively by the direct pressor action of the concomitant increase in plasma angiotensin II (Caravaggi *et al.*, 1976). Later in the course of hypertension, peripheral plasma concentrations of angiotensin II are lower in relation to arterial pressure (Brown *et al.*, 1979) and it is in this second phase that renovascular hypertension is usually first encountered in man. It is rare clinically to observe the evolution of renal artery stenosis with hypertension, and detailed biochemical assessment before and after the development of such a lesion has not, to our knowledge, been reported previously. The following account describes the development of unilateral renal artery stenosis and severe hypertension in a patient in whom detailed investigations one year earlier had disclosed no relevant abnormality.

Case report

The patient, a 33-year-old labourer, first presented in February 1976 with a subarachnoid haemorrhage

caused by a ruptured berry aneurysm of the posterior communicating artery. At craniotomy clipping of the aneurysm was technically impossible. After the operation his blood pressure was 150/106 mmHg. Propranolol (80 mg daily) was introduced as an out-patient and blood pressure control was good, averaging 120/78 mmHg on four visits to his general practitioner.

In February 1977 the patient was referred to the MRC Blood Pressure Unit for assessment and after one month without treatment he was admitted for investigation. Arterial pressure was then 140/102 mmHg (mean of six readings) and his optic fundi were normal. Physical examination did not demonstrate any cause for the increase in blood pressure. He smoked 20 cigarettes a day. There was no family history of hypertension, though his father had died, aged 51, after a myocardial infarction. Investigation (March 1977) in the metabolic ward on a fixed known and normal intake of sodium and potassium, revealed in samples taken at 08.30 a.m., after overnight recumbency and fasting, normal serum electrolytes (sodium 142 mmol/l, potassium 4.3 mmol/l, bicarbonate 24 mmol/l) and peripheral plasma concentration of active renin—18 μ U/ml (normal range 9–50 μ U/ml; Millar *et al.*, 1978), angiotensin II—19 pmol/l (normal range 5–35 pg/ml; Dusterdieck and McElwee, 1971), and aldosterone—11 ng/100 ml (305 pmol/l) (normal

range < 18 ng/100 ml (< 499 pmol/l); Fraser *et al.*, 1973). Other normal results were blood urea (4.2 mmol/l) and creatinine (86 μ mol/l), creatinine clearance (85 ml/min), fasting lipids, urinary normetadrenaline, electrocardiogram, and chest x-ray. Exchangeable sodium and potassium were 91.7 per cent and 99.2 per cent of the expected values, respectively (Davies and Robertson, 1973). An intravenous pyelogram was normal, apart from a suspicion of a small calyceal cyst on the right side. Because of this finding and the patient's age, plasma concentrations of renin and angiotensin II were estimated in blood samples taken from the renal veins (Semple *et al.*, 1979) and these were normal with no suggestion of a unilateral lesion (Table 1).

After discharge from hospital, blood pressure was well controlled by propranolol (80 mg daily): April 1977, 136/84 mmHg; August 1977, 134/86 mmHg; October 1977, 140/88 mmHg; and February 1978, 136/86 mmHg. However, at his next outpatient visit in May 1978, after severe frontal headaches for three weeks, he was readmitted with a blood pressure of 210/144 mmHg and bilateral retinal haemorrhages and exudates, though no papilloedema were present. Blood pressure was reduced, but not to normal (176/108 mmHg, mean of 10 readings) with atenolol (200 mg daily), minoxidil (20 mg daily), and frusemide (80 mg daily).

His intravenous pyelogram now showed typical features of right-sided renal artery stenosis (Brown

et al., 1960) with delayed excretion of contrast on the right side and with increased concentration of dye both before and after a water load. Arteriography confirmed that he had developed a tight 1 cm long stenosis beginning 4 mm from the origin of his right renal artery. Repeat renal vein sampling (Table 1) then showed a distinct excess of renin in plasma from the right renal vein contrasted with the negative venoarterial difference across the left kidney, indicating net extraction of renin by the unaffected contralateral kidney. Angiotensin II levels in renal vein plasma were also consistently higher on the right than on the left. These were, therefore, classical findings of unilateral renal artery stenosis (Millar *et al.*, 1978; Semple *et al.*, 1979). Divided renal function studies (Table 2) also showed changes characteristic of right renal artery stenosis (Brown *et al.*, 1960).

In an effort to correct the hypertension, a right aortorenal bypass graft was inserted in June 1978 but the graft thrombosed within five days and his blood pressure remained high. The infarcted right kidney was removed one week later. The blood pressure fell by 10 days after nephrectomy to 164/104 mmHg and was controlled easily with atenolol 100 mg daily. Three months after operation beta-adrenergic blockade was withdrawn and blood pressure thereafter remained consistently less than 140 mmHg systolic, 90 mmHg diastolic. Six months after the operation, repeat estimations of peripheral plasma concentrations of active renin, 24 μ U/ml,

Table 1 Renal vein sampling

	Active renin (μ U/ml)						Angiotensin II (pmol/l)					
	March 1977			May 1978			March 1977			May 1978		
	Samples			Samples			Samples			Samples		
	1	2	3	1	2	3	1	2	3	1	2	3
Left renal vein	14	16	16	344	308	372	13	13	14	39	40	48
Right renal vein	15	15	17	535	902	999	15	13	18	52	80	68
Aorta	15	14	16	360	347	467	14	17	15	71	89	90

Active renin levels (normal range 9 to 50 μ U/ml) and angiotensin II levels (normal range 5 to 35 pmol/l) on simultaneous sampling from the left renal vein, right renal vein, and aorta. In March 1977 the patient was on no drugs, in May 1978 he was on frusemide, prazosin, and hydralazine.

Table 2 Divided renal function study

Plasma Creatinine μ mol/l	PAH μ mol/l	Period		Urine		Na ⁺		Creat.		PAH		C _{Cr}		C _{PAH}	
		No.	Min	ml/min	R	L	R	L	R	L	R	L	R	L	R
112	97	1	4	8.1	2.4	60	27	0.88	1.67	4.30	9.18	64	36	359	227
104	105	2	4	9.5	2.6	50	18	0.89	1.71	4.44	9.64	81	43	402	239
107	115	3	4	8.0	2.6	50	34	0.81	1.22	4.00	6.76	61	30	278	153
104	118	4	4	8.5	2.6	45	17	0.81	1.45	4.20	8.10	66	36	303	178

Note: The lower urine volume and sodium concentration on the right and the higher creatinine and PAH concentration are typical of right renal artery stenosis (Brown *et al.*, 1960).

angiotensin II, 20 pmol/l, and aldosterone, 8 ng/100 ml (222 pmol/l) were all normal in samples obtained in recumbency.

Discussion

As far as we are aware, detailed assessment of the renin-angiotensin-aldosterone system, and in particular renal vein renin and angiotensin II values, have not been described previously in man before and after a renal artery stenosis of rapid onset. However, Adams and Newman (1958), Laidlaw *et al.* (1960), and Barraclough (1966) describe patients in whom hypertension secondary to renal artery stenosis was noted from 42 days to four months after blood pressure was known to be normal. All of those cases presented with loin pain, suggesting renal infarction, but no such symptoms were present in this case. Our patient previously had a subarachnoid haemorrhage, but since the increased blood pressure associated with that syndrome (Neil-Dwyer and Cruickshank, 1974) is usually short-lived and investigation disclosed no other cause, continuing mild hypertension after craniotomy was not thought to be related to this.

The cause of this patient's renal artery stenosis has not been determined. Arteriographic findings were not typical of fibromuscular hyperplasia and no changes were shown in any other vessels, though the stenosed area was not available for histological examination. Family and smoking histories make atheroma, with or without thrombus formation, the likely cause, though the aorta was not noted to be atheromatous at arteriography.

There is good evidence that the early rise of blood pressure occurring in animals after clipping a renal artery is a result of the associated increase in plasma concentrations of renin and angiotensin II (Caravaggi *et al.*, 1976; Brown *et al.*, 1979). In man, observations before a stenosis develops can only be fortuitous, as in the case described above, where the results of renal vein sampling (Table 1) are consistent with the animal model. Normal blood pressure accompanied normal peripheral plasma renin and angiotensin II after nephrectomy. Rapid loss of blood pressure control (in less than three months) with potentially disastrous cerebral consequences was thus corrected in this young patient by removal of the source of excess renin secretion.

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