CLINICAL REPORTS

Renovascular hypertension associated with bilateral aldosteronoma

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Summary

The authors present a 35-year-old male patient with renovascular hypertension caused by the stenosis of both renal arteries of the right kidney. Two years after the diagnosis of hypertension was made, an endarterectomy was performed but a successful correction of the upper stenotic artery was not achieved. During the next 2 years the hypertensive disease was uncontrollable with antihypertensive medications and gradually entered into a malignant phase. In addition to the atrophy of the right kidney, an adenoma of the left adrenal gland was revealed (19.75 g) which was operated on. Left adrenalectomy had only a transitory benefit on blood pressure level. Five months later an adenoma of the right adrenal gland was diagnosed and together with the ischaemic right kidney was operated on (right adrenalectomy and nephrectomy) which definitely cured the hypertension.

The chronological sequence of events and the course of the disease in the patient point to the possibility that long-standing hyper-reninaemia, due to renal ischaemia, may cause the development of multiple bilateral adrenocortical adenomas and that secondary aldosteronism may transform into primary.

KEY WORDS: primary adenomatous aldosteronism, renovascular hypertension, nephrectomy, adrenalectomy.

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Introduction

The simultaneous occurrence of adrenocortical adenoma and renovascular hypertension has been reported in a few cases (Laidlaw, Yendt and Gernerl, 1960; Hoet and Molinaeaux, 1960; Mills *et al.*, 1980). The corrective surgery of unilateral renal artery stenosis and the operation on the secretory adrenal tumour resulted in the cure of arterial hypertension in one patient (Mills *et al.*, 1980).

In 1964 Conn, Cohen and Rouner pointed to the theoretical possibility of the simultaneous occurrence of renovascular hypertension and aldosteronism being due to an aldosterone-producing adenoma.

'Secondary primary', 'tertiary' and 'autonomous secondary' aldosteronism are synonyms. They are used to describe a disorder in a small group of patients in whom a secretory active adrenocortical adenoma has developed as a result of a long acting stimulus for aldosterone secretion (Ross, 1975).

Case report

A 29-year-old male patient presented in 1975 with headache and hypertension. His blood pressure was found to be 160-180/100-130 mmHg. Routine laboratory examinations were within normal ranges. No hormonal analyses were performed at that time.

In 1977 selective renal angiography revealed two renal arteries for the right kidney, both of which showed stenosis. An endarterectomy was performed in November 1977 but did not result in a decrease in blood pressure.

Over the next 2 years the patient remained

hypertensive. His blood pressure was 190–250/120–170 mmHg despite therapy with methyl-dopa, 750–1500 mg/day, and propranolol 240 mg/day. Aortography and renal angiography revealed occlusion of the superior renal artery, sclerosis of the right kidney and dissection of the abdominal aorta at the site of clamping during the previous endarterectomy. Arteriography did not demonstrate an adrenal tumour. Selective catheterization of the renal veins in August 1979 showed bilateral increased levels of plasma renin activity.

In December 1979 the patient was admitted to the Endocrinology Department of the City Clinic Hospital for the first time. His major symptoms were headache, thirst and excessive diuresis. He appeared chronically ill, with a pale, dry skin. His blood pressure was 200/110 mmHg and pulse rate 86/min. The fundi revealed hypertensive retinopathy grade II. The chest radiograph and electrocardiogram showed evidence of left ventricular hypertrophy.

Investigations

Plasma aldosterone and angiotensin I levels were determined by the antibody-coated tube method (RIA), using a CIS-SORIN test kit.

Samples for plasma renin activity (PRA) were collected with a cold syringe and mixed with 6% cold EDTA (0.15 ml EDTA per 10 ml blood), and after centrifugation stored at -20°C until assayed. The generation of angiotensin I was run at pH 7.4 for 3 hr.

Scintigraphy of the adrenal gland was performed using $^{75}\text{selenocholesterol}$ (Scintandren, Amersham) on the 5th day following the application of the agent.

Normal values of plasma aldosterone were 0.03–0.35 nmol/l (supine) and 0.19–0.82 nmol/l (upright) and of plasma renin 0.08–1.37 nmol/l/hr (supine) and 0.63–2.69 nmol/l/hr (upright).

Blood urea 4.5 mmol/l and creatinine 118.5 $\mu\text{mol/l}$, serum potassium 3.1–3.7 mmol, serum sodium 137–143 mmol. Urine volume was 1,800 and 3,500 ml/24 hr, urinary potassium loss 70–150 mmol/24 hr and sodium loss 150–300 mmol/24 hr, on an ordinary hospital diet. Plasma ACTH and cortisol levels, 24 hr urinary 17-hydroxycorticosteroids, adrenaline, noradrenaline and vanillylmandelic acid excretion were normal. Increased plasma renin activity and high plasma aldosterone levels were consistent with secondary aldosteronism (Fig. 1.).

In May 1980 computed tomographic scan, echography and scintigraphy of the adrenal glands were consistent with a left adrenal tumour.

Further course

In August 1980 a total left adrenalectomy was performed. Histopathological examination showed

an aldosteronoma (19.75 g) with smaller aldosteronoma near by together with areas of hyperplasia in the zona fasciculata of the remaining cortex. On the fourth and seventh post-operative days the plasma renin activity was raised at 7.8 nmol/l/hr and the plasma aldosterone at 2.35 nmol/l respectively.

During the 6-week period after surgery the patient responded relatively well to the treatment with methyl-dopa, 750 mg per day, and propranolol, 120–240 mg per day, but after that period he again became hypertensive (Fig. 1).

In October 1980 the patient was readmitted. His symptoms were intermittent generalized muscular weakness, cramps in both legs and headache. Plasma renin activity and plasma aldosterone levels were extremely high at that time and during the following months (Fig. 1). Scintigraphy revealed a tumour of the right adrenal gland.

In May 1981 the patient underwent his third operation: right adrenalectomy and right nephrectomy. Histological examination revealed a 12 mm aldosteronoma with three further microadenomata on histology, as well as changes in the parenchyma of the kidney consistent with the malignant phase of arterial hypertension.

Post-operatively blood pressure fell to within normal limits without antihypertensive medications, treatment being limited to hormonal replacement therapy with hydrocortisone 30 mg per day. Plasma renin activity and plasma aldosterone levels have since remained within normal limits.

Discussion

Adenomatous primary aldosteronism can be differentiated from renovascular hypertension by its clinical manifestations and the results of biochemical investigations (Biglieri, Stockigt and Schambelan, 1972; Laragh *et al.*, 1972; Mantero *et al.*, 1978; Wolfsen, Tuck and Kaplan, 1977).

If however renovascular disease has entered into an accelerated or malignant phase then the clinical manifestations of adenomatous primary aldosteronism and renovascular hypertension become almost indistinguishable (Laidlaw *et al.*, 1960; Mičić *et al.*, 1967; Laragh *et al.*, 1972; Clarke *et al.*, 1979; Atkinson *et al.*, 1979). However, the estimation of the plasma angiotensin and aldosterone levels in the peripheral blood as well as in the renal veins makes it possible to differentiate between the two diseases (Conn *et al.*, 1964; Biglieri *et al.*, 1972; Laragh *et al.*, 1972; Ross, 1975; Wolfsen *et al.*, 1977). Table 1 shows the essential clinical and biochemical characteristics of primary adenomatous aldosteronism and renovascular hypertension, together with findings in our patient in December 1979.

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FIG. 1. The levels of serum sodium, serum potassium, plasma aldosterone, plasma renin activity (PRA), blood pressure and applied treatment before and after operations. OP I—left adrenalectomy; OP II—right adrenalectomy and right nephrectomy.

The contribution of aldosteronomas to the pathogenesis of the patient's hypertension was partially removed by left adrenalectomy, in August 1980 (OP I, Fig. 1). The increased plasma renin activity found in the peripheral blood on the fourth postoperative day was followed by a significant increase in the plasma aldosterone level. The removal of the left adrenal adenoma resulted in the elimination of the

suppressive effects of aldosterone on the production of plasma renin, which had already been at an increased level before surgery.

The following observations are consistent with the hypothesis that renal ischaemia of long duration resulted in the development of multiple bilateral adrenocortical adenomas:

- (1) The existence of malignant hypertension which

TABLE 1. The essential clinical and biochemical characteristics of primary adenomatous aldosteronism (PAA), renovascular hypertension (RVH) and the patient

	PAA	RVH	Patient
Polyuria	+	+	+
Polydipsia	+	+	+
Serum potassium	↓	↓	↓
Serum sodium	↑	N or ↓	↓
Plasma renin	↑	↑	↑
Plasma aldosterone	↑	↑	↑

was uncontrollable with antihypertensive treatment.

- (2) The first scintigraphy revealing only the adenoma in the left adrenal gland and not in the right one (May 1980).
- (3) The lack of effect of the removal of the left adrenal gland on the arterial hypertension.
- (4) The appearance of adenoma in the right adrenal gland 5 months following the first scintigraphy (October 1980).
- (5) The definitive curative effect of the right nephrectomy and adrenalectomy.

It is not known what the effect of a right nephrectomy, before the first and particularly before the second adrenalectomy, would have been; i.e. if the removal of the ischaemic kidney would have prevented the development of the right adrenal adenomas.

It is possible that primary and secondary aldosteronism were simultaneously present in our patient, which implies the coincident occurrence of both renovascular disease with hypertension and primary adenomatous aldosteronism. However it seems likely that the course of the disease and the results of investigations are consistent with 'secondary primary' aldosteronism, i.e. the transformation of secondary aldosteronism into primary.

Finally we would like to emphasise that in treating hypertensive disease special attention should be paid to prevent the possible development of

adrenocortical adenoma in particularly sensitive patients.

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