A Case of Primary Aldosteronism with Renovascular Hypertension

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A case of primary aldosteronism associated with renovascular hypertension is reported. The patient, a 46-year-old woman, developed hypertension to the level of 210/110 mmHg. Laboratory data included serum potassium 3.4 mEq/l, plasma renin activity 25 ng/ml/h and plasma concentration of aldosterone 330 pg/ml. Occlusion of the left renal artery and left adrenal aldosteronoma was diagnosed by radiographic and hormone analysis findings. Left adrenalectomy and nephrectomy corrected the hypertension. The possibility of tertiary aldosteronism is discussed.

Key words: Angiotensin II

Secondary aldosteronism is known to occur in renovascular hypertension. It is well known that in many hormone producing organs, autonomous hormone production can develop after sustained stimulation of hormone secretion, such as in hyperparathyroidism. In this paper, we describe a case of primary aldosteronism with renovascular hypertension and discuss the pathogenetic relationship of these two diseases.

CASE REPORT

In 1982, a 46-year-old woman was found to have high blood pressure (160/100 mmHg), but she denied medication. In 1984, she was admitted to our hospital because of severe headaches and weakness in all four extremities. In the past, she underwent removal of right adnex due to ectopic pregnancy and medical treatment for peptic ulcer. Physical examination on admission was negative except for the elevation of blood pressure (210/110 mmHg) and hypertensive change in retina (Keith-Wagener III). Neurological examination showed clear consciousness and normal cranial nerve function. Deep tendon reflexes were slightly diminished in all extremities, however muscle strength seemed to be normal.

Laboratory findings included normal urine, normal blood counts, a slight decrease in serum potassium (3.4 mEq/l) and elevation in fasting blood glucose (117 mg/dl). Hormonal evaluation revealed the elevation of plasma renin activity (25 ng/ml/h) and aldosterone concentration (330 pg/ml). A circadian rhythm of aldosterone was not found (245 pg/ml at 8 AM, 290 pg/ml at 4 PM). Abdominal computed tomography revealed atrophy of the left kidney and a left adrenal tumor (Fig. 1). Aortography showed complete occlusion of the left renal artery from its origin (Fig. 2). Venography confirmed the left adrenal tumor (Fig. 3). A venous sampling study demonstrated the elevation of plasma renin activity in left renal venous blood and a selective increase in plasma aldosterone concentration in the left adrenal vein (Table 1). From these results, the diagnosis of renovascular hypertension and primary aldosteronism was made.

For treatment, left adrenalectomy and nephrectomy were carried out. The removed kidney...
Fig. 1. Abdominal computed tomography revealed atrophy of the left kidney and a left adrenal mass.

Fig. 2. Aortography revealed the complete occlusion of the left renal artery and some collateral vessels.

Fig. 3. Venography confirmed the presence of the left adrenal tumor (2 x 2 cm).

Table 1. The hormonal values in venographic samples.

<table>
<thead>
<tr>
<th></th>
<th>PRA (ng/ml/h)</th>
<th>PAC (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior vena cava</td>
<td>19</td>
<td>290</td>
</tr>
<tr>
<td>(suprarenal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left adrenal vein</td>
<td>21</td>
<td>&gt; 4000</td>
</tr>
<tr>
<td>Left renal vein</td>
<td>&gt; 25</td>
<td>560</td>
</tr>
<tr>
<td>Right renal vein</td>
<td>21</td>
<td>190</td>
</tr>
<tr>
<td>Inferior vena cava</td>
<td>18</td>
<td>180</td>
</tr>
<tr>
<td>(infrarenal)</td>
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PRA = plasma renin activity, PAC = plasma concentration of aldosterone. All blood samples were collected in the venographic examination.

Fig. 4. Gross pathology of the removed left renal tissue weighing 45 g.

was 45 g and renal artery was occluded by atherosclerosis and thrombus, which was confirmed by the operation (Fig. 4). The tumor in the left adrenal gland weighed 10 g and light microscopic examination revealed that the adenoma consisted of predominantly clear cells with no malignant picture (Fig. 5). After operation, her blood pressure was normalized without medication (134/80 mmHg). The serum potassium (4.9 mEq/l), plasma renin activity (1.0 ng/ml/h) and plasma concentration of aldosterone (64 pg/ml) were also normalized one month after the operation.
Aldosteronoma in Renovascular Disease

Fig. 5. The microscopic appearance of the removed adrenal tumor. The tumor consisted predominantly of clear cells (×40).

DISCUSSION

The present case was considered to be compatible with left renovascular hypertension associated with left adrenal aldosteronoma. The preferential elevation of plasma renin activity in left renal venous blood and the increase in the plasma concentration of aldosterone in the left adrenal vein would support the diagnosis. It should be emphasized that radiologically the left renal artery was occluded from the origin and that we could not find any bruits or inflammatory signs (negative C-reactive protein). The lesion of the renal artery was thus thought to be atherosclerotic and was then confirmed by the intra-operative findings. Schreiber et al (1) reported that in 46% of patients it takes 2 years for renal arterial stenosis to progress to occlusion. In this patient, hypertension developed about 2 years prior to admission and was completely corrected by surgical intervention. Although we did not examine her renin value previously, it seems reasonable to postulate that renovascular stenosis caused the initial elevation of her blood pressure. The possibility of pre-existing aldosteronoma was unlikely for various reasons. One reason is the late appearance of symptoms associated with hypokalemia, such as muscle weakness and headache, a major symptom of primary aldosteronism. Another reason is that severe hypertensive change in the retina as observed in this case has been demonstrated in few cases of primary aldosteronism (2).

The simultaneous occurrence of adrenocortical adenoma and renovascular hypertension has been reported (3–8). Vircburger et al (5) reported the development of bilateral aldosteronoma followed by long-standing renovascular hypertension with hyperreninemia. Angiotensin II is a well-known peptide which stimulates the secretion of aldosterone from the adrenal glands and causes vasoconstriction through the breakdown of phosphatidylinositol (9, 10). A recent investigation revealed that angiotensin II promotes the growth and proliferation in cultured vascular smooth muscle cells (11). Angiotensin II was also reported to induce the expression of oncogenes, such as c-myc (12). Since angiotensin II would activate a similar second messenger system in smooth muscle and zona glomeruloza cells, it seems feasible to consider that the prolonged elevation of angiotensin II observed in renovascular hypertension could generate aldosteronoma. In this case, numerous clear cells were seen in the non-tumorous region of the adrenal gland and no capsulation was seen surrounding the tumor (Fig. 6). These findings might reflect the genesis of clear-cell type aldosteronoma by the sustained stimulus of angiotensin II to adrenal glands. The bilateral adenomas were observed in the case of Vircburger (5), while a unilateral adenoma was seen in the present case. The reason for this difference was not clear. However, it should be noted that the bilateral adenomas were detected 5 years after the discovery of hypertension and that in the present case the tumor developed in only 2 years. This disparity in the duration might explain the difference in

Fig. 6. The microscopic appearance of the non-tumorous region of the removed adrenal gland. Clear cells were predominant (×40).
Ross (13) proposed the idea of secondary-primary or tertiary aldosteronism to describe aldosteronoma which develops as a result of a long-acting stimulus. His idea seemed foresighted because he advocated this in 1975, when the mechanism of action of angiotensin II was not known. The present case appears to support the proposal of Ross and suggests that pathologically elevated angiotensin II might contribute to the occurrence of aldosteronoma.

REFERENCES