Renin-Secreting Tumor

Case Report

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SUMMARY  Renin-secreting tumor, though rare, should be considered in assessing severe hyperreninemic, hypertensive patients. We studied an 18-year-old girl with hypokalemic hyperreninemic hyperaldosteronism. No angiographic lesion could be detected. The plasma renin activity (PRA) of the right/left renal vein was 73. With a presumptive diagnosis of renin-secreting tumor (RST), the patient was operated on, and a cortical nodule was found on the right lower pole. Partial nephrectomy was followed by a rapid fall in PRA (half-life, 33-44 min) and normalization of blood pressure (BP). At 3½ months postoperatively, the patient showed normotension, normokalemia, normal aldosterone, and slightly elevated PRA unresponsive to postural changes and furosemide treatment. Tumoral PRA secretion responded to postural stimulus, spironolactone use, and nitroprusside-induced hypotension. Neither the high aldosterone excretion nor hyperreninemia decreased after 3 days of DOCA; this agrees with a previously reported case suggesting the usefulness of this test in the diagnosis of RST. (Hypertension 2: 714-718, 1980)

KEY WORDS  •  renin-secreting tumor  •  hyperreninemia  •  deoxycorticosterone acetate (DOCA)  •  kidney function  •  spironolactone  •  furosemide  •  plasma renin activity

ELEVEN years after the first case was reported by Robertson et al.,1 renin secreting tumor (RST) continues to be a rare cause of curable hypertension. Initial cases were diagnosed by the postsurgical histological study,1-3 and the most recent ones have been recognized preoperatively.4-11 We describe an additional case in which a presumptive diagnosis was made preoperatively, facilitating removal of the tumor and subsequent rapid and sustained normotension.

Case Report

An 18-year-old white girl was referred to the Catholic University Hospital because of hypertension of 2 years' duration. Her complaints were headaches, leg cramps, easy fatigability, polydipsia, and nocturia. Two years before admission, no abnormalities had been detected in renal function, rapid sequence intravenous pyelogram, and renal arteriogram. At that time plasma sodium and potassium levels were 138 and 3.3 mEq/liter respectively, with a 24-hour urinary excretion of sodium 110 mEq and potassium 21 mEq. Guanethidine, methyldopa, and propranolol in combination with diuretics were used in maximally tolerated doses and failed to control arterial pressure.

The physical examination showed a young female in no acute distress whose weight was 50 kg and whose height was 158 cm. Blood pressure was 220/150 mm Hg in both supine and upright position and was not changed by abdominal palpation. Heart rate was regular, 80/min supine and 120/min upright. The fundoscopic examination showed intensely vasoconstricted arteries with increased light reflex (2+), scarce small exudates, and retinal and papillary edema.

Laboratory work-up was performed under balance conditions on a daily intake of 120 mEq sodium and 70 mEq of potassium. All medication had been discontinued 3 weeks before admission. Plasma and urinary aldosterone were measured by radioimmunoassay;12,13 plasma renin activity (PRA) was...
determined using a commercially available kit from New England Nuclear.

Results obtained are the following: hematocrit 42%, BUN 15 mg/dl, creatinine clearance 89 ml/min, plasma creatinine 0.8 mg/dl. The electrocardiogram, serum albumin, total protein, calcium phosphate, uric acid, cholesterol, alkaline phosphatase, LDH, SGOT, and cortisol were all normal, as were urinary 17-hydroxisteroid, 17-ketosteroid, epinephrine and norepinephrine excretion rates. A renal arteriogram showed no abnormalities. Maintained hypokalemia, kaliuresis, elevated urinary aldosterone, and hyperreninemia were observed under balance (basal) conditions (table 1). Supine plasma aldosterone concentration was 13 ng/dl (normal = 3-31.4 ng/dl). Under the same dietary conditions, 3 days of deoxycorticosterone acetate (DOCA), 10 mg intramuscularly twice per day, did not change body weight, arterial pressure, PRA, or urinary aldosterone excretion rate (table 1).

The patient was treated for 2 months with spironolactone, 250 mg/day. Although arterial blood pressure (BP) remained at 220/150 mm Hg she felt considerably improved, with disappearance of cramps and fatigue. On readmission to the hospital, laboratory work-up performed under balance conditions during spironolactone therapy revealed normokalemia and further increases in PRA and urinary aldosterone excretion rate (table 1).

Renal venous blood samples were obtained in the supine position before and after nitroprusside-induced hypotension (table 2). The PRA ratio of the right/left renal vein was 7.3; PRA of the left renal vein was the same as that of the inferior vena cava in either condition. Despite important percentual increments in PRA from both sides after stimulation, identity between the PRA of the left renal vein and inferior vena cava points to a negligible renin secretion from the left kidney.

A working diagnosis of RST of the right kidney was made, and at operation a whitish tumor 15 mm in diameter was found in the lower pole; subtotal nephrectomy was done. Surgical exploration of adrenal glands revealed no abnormalities.

Light microscopy demonstrated a well-defined compact tumor composed of ovoidal and fusiform cells with no atypical cells (fig. 1). Bowie's stain was positive; no nerve fibers were found with the modified Chen-Bodian stain. The adjacent renal cortex had arteriolosclerosis with hyalinization and signs of focal and segmental ischemia in 10% of the glomeruli. The count of juxtaglomerular cells was normal according to Turgeon-Sommers technique. Electron microscopy showed three types of cytoplasmic granules: crystalloid, homogeneous, and fibrilar. The endoplasmic reticulum was rugged and dilated. Homog-

### Table 1. Responses of Plasma and Urinary Sodium (Na) and Potassium (K), Peripheral Plasma Renin Activity (PRA), and Aldosterone Excretion Rate (AER) in an 18-Year-Old Girl with a Renin-secreting Tumor

<table>
<thead>
<tr>
<th>Condition</th>
<th>Plasma Na/K (mEq/liter)</th>
<th>Urinary Na/K (mEq/24 hrs)</th>
<th>PRA Recumbent (ng/ml/hr)</th>
<th>PRA Standing (ng/ml/hr)</th>
<th>AER (ug/24 hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>146 2.8</td>
<td>128 104</td>
<td>0.7-2.4</td>
<td>1.1-7.8</td>
<td>4-14</td>
</tr>
<tr>
<td>DOCA</td>
<td>146 3.0</td>
<td>128 101</td>
<td>17.4</td>
<td>41.5</td>
<td>15.5</td>
</tr>
<tr>
<td></td>
<td>142 2.9</td>
<td>129 105</td>
<td>32</td>
<td>50</td>
<td>13.8</td>
</tr>
<tr>
<td></td>
<td>143 2.8</td>
<td>100 95</td>
<td>64</td>
<td>144</td>
<td>56.4</td>
</tr>
<tr>
<td></td>
<td>140 4.3</td>
<td>84 98</td>
<td>66</td>
<td>66</td>
<td>80.7</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>140 4.2</td>
<td>114 75</td>
<td>0.3</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>143 4.1</td>
<td>69 23</td>
<td>1.3</td>
<td>2.9</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>143 3.8</td>
<td>55 84</td>
<td>2.6</td>
<td>9.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>139 3.8</td>
<td>100 91</td>
<td>3.7</td>
<td>2.8</td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td>3.6</td>
<td>4.3*</td>
<td>14.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Furosemide, 20 mg, administered intravenously.

### Table 2. Bilateral Renal Vein Plasma Renin Activity During Basal Conditions and after Sodium Nitroprusside (NPS)—Induced Hypotension

<table>
<thead>
<tr>
<th>Condition</th>
<th>BP (mm Hg)</th>
<th>RRV</th>
<th>LRV</th>
<th>IVC</th>
<th>PRA RRV</th>
<th>PRA LRV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>210/150</td>
<td>704</td>
<td>96</td>
<td>96</td>
<td></td>
<td>7.3</td>
</tr>
<tr>
<td>NPS infusion</td>
<td>100/60</td>
<td>1052</td>
<td>132</td>
<td>132</td>
<td></td>
<td>8.0</td>
</tr>
<tr>
<td>% Increment</td>
<td>49</td>
<td>37</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RRV = right renal vein; LRV = left renal vein; IVC = inferior vena cava.
Figure 1. Tumoral tissue with two sinusoidal vascular structures (S). (Epon and toluidine blue, × 500).

Enous dense zones were found in the intercellular spaces. Nerve fibers were not detected by this technique (fig. 2).

Figure 3 shows the rapid fall in PRA and arterial pressure following tumor resection. As BP stabilized at 90/60 mm Hg 9 hours after resection and was accompanied by symptoms and signs of low peripheral perfusion, 500 ml of whole blood were transfused, obtaining a rise to 130/90 mm Hg. Thereafter, arterial BP showed a fluctuating pattern with a descending trend, attaining stable normotension 7 days after operation. The postoperative course was uneventful, and the patient was discharged on the 11th postoperative day normokalemic and normoreninemic. Monthly arterial pressure readings were normal, averaging 120/70 mm Hg.

The patient was readmitted 3½ months after operation and showed under balance conditions normokalemia, slightly elevated PRA with no response to the upright position, and a poor response to the combined postural and furosemide stimulus. A low normal urinary aldosterone excretion rate was also demonstrated, with a minimal increase over the normal range when challenged by furosemide.

Figure 2. Electron micrograph of tumoral cell showing nucleus (Nu), homogeneous and crystalloid granules (gr), rugged and dilated cytoplasm (rend), and dense intercellular zones (*). (× 8,000).
Discussion

Although RST is a rare cause of curable severe hypertension, it should be incorporated as working diagnosis in hyperreninemic hypertensive patients. The tumor is not always disclosed by renal arteriogram, due to its small size, and bilateral sampling from renal veins may be required for PRA determination. The pathological description of benign tumors in all reported cases prompted us to perform partial nephrectomy which we believe should be the procedure of choice whenever feasible.

Tumoral secretory capacity was stimulated by the erect position, spironolactone use, and nitroprusside-induced hypotension, indicating its dependence on both autonomic stimuli and volume changes, as previously described. Failure of DOCA to suppress PRA does not deny tumoral volume responsiveness. In our patient, no volume expansion could be sustained since a brisk sodium escape was observed and weight remained unchanged. We estimate that the DOCA maneuver might be of diagnostic value in this entity, as suggested by Schambelan et al. in 1973, since this test has been consistent in its ability to suppress all forms of secondary hyperaldosteronism.

After tumoral resection, PRA fell to 50% within 33 minutes of the first hour and at 44 minutes during the following 1½ hours. These values agree with those previously reported. On the third postoperative day, PRA levels and the aldosterone excretion rate were depressed, mimicking the response observed after resection of aldosterone-producing adenomas. Prolonged volume expansion has been invoked as the suppressive mechanism, but prolonged spironolactone use should produce some degree of volume depletion, as in our patient. The immediate postoperative PRA levels can be attributed to the inhibition exerted in the preoperative period by the high levels of angiotensin II. The importance of this renin-angiotensin feedback is supported by the pre-operative lack of renin output from the contralateral kidney under spironolactone therapy and subsequent induced hypotension. Normalization of supine PRA was achieved on the 9th postoperative day. The slightly high supine PRA found 3½ months after surgery could be attributed to a maintained basal stimulation secondary to the already present vascular damage. However, the hyporesponsiveness to postural stimulus and furosemide indicates that a complete normalization of the renin-angiotensin system has not been attained. This could account for the low normal aldosterone excretion rate and its blunted response to furosemide.

Basal plasma and urinary aldosterone were not as high as expected for such high PRA values, but this can be ascribed to the persistently low plasma potassium concentration. When normokalemia was achieved by the chronic administration of spironolactone, a significant rise in urinary aldosterone excretion was observed. The fixed aldosterone excretion under DOCA effect, while PRA increased, could be reported to depress aldosterone synthesis.

Acknowledgments

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References

9. Orijavik OS, Aas M, Fauschald P, Howig T, Oytesse B, Brodwall EK, Flatmark A: Renin secreting renal tumor with severe...
Renin-secreting tumor. Case report.
G Valdés, J M Lopez, P Martinez, H Rosenberg, P Barriga, J A Rodriguez and N Otipka

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