Unusual Association of Hyperkalemia and Hypertension

ESA SOPPI, JORMA VIJKARI, PENTTI SEPPÄLÄ, AAPO LEHTONEN, RIITTA SAARINEN, AND SEppo MIILUNPALO

SUMMARY We report an unusual association of hyperkalemia, mild hyperchloremic acidosis, and hypertension in a young woman. Pseudohyperkalemia, Addison's disease, renal insufficiency, classical hyperreninemic hyperaldosteronism, isolated hyperaldosteronism, and iatrogenic causes were excluded. The patient's findings were compatible with a rare syndrome designated as type II pseudohypoaldosteronism, Gordon's syndrome. (Hypertension 8: 174–177, 1986)

KEY WORDS hyperkalemia hypertension pseudohypoaldosteronism Gordon's syndrome

The primary investigation of the hypertensive patient includes the determination of serum electrolyte levels in expectation that hyperpotassemia will reveal any instances of the rare but curable condition, primary hyperaldosteronism. Persistent hyperpotassemia accompanied by hypertension in the absence of oliguria or severe renal failure is an unusual biochemical finding. When pseudohyperkalemia, Addison's disease, hyperreninemic hyperaldosteronism, isolated hyperaldosteronism, and iatrogenic causes are excluded, a real association of hyperkalemia and hypertension should be considered.

We describe a patient with persistent hyperkalemia, hyperchloremic acidosis, and hypertension whose findings are compatible with a syndrome designated as type II pseudohypoaldosteronism (Gordon's syndrome). In a review of the medical literature, we could find only 11 previous reports of type II pseudohypoaldosteronism (Table 1).2-14

Case Report

A girl born in 1964 was admitted to the department of pediatrics of a local university hospital in 1979 because of hypertension (150–160/110–125 mm Hg). Subsequent examinations were conducted in the department of medicine. She had a family history of hypertension (father, father's sister, and paternal grandfather). Her mother had had hypertension and proteinuria during pregnancy. Her sister had been observed for borderline blood pressure values. Childhood diseases included chicken pox, varicella, and measles.

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (yr)/sex</th>
<th>BP (mmHg)</th>
<th>GFR (mL/sec/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paver and Pauline, 1964</td>
<td>21/M</td>
<td>180/120</td>
<td>1.9</td>
</tr>
<tr>
<td>Stokes et al., 1968</td>
<td>10/F</td>
<td>160/110</td>
<td>1.7</td>
</tr>
<tr>
<td>Arnold and Healy, 1969</td>
<td>11/M</td>
<td>110/70</td>
<td>0.6</td>
</tr>
<tr>
<td>Gordon et al., 1970</td>
<td>9/M</td>
<td>105/65</td>
<td>1.8</td>
</tr>
<tr>
<td>Spitzer et al., 1973</td>
<td>52/M</td>
<td>200/100</td>
<td>2.2</td>
</tr>
<tr>
<td>Weinstei n et al., 1974</td>
<td>48/M</td>
<td>?/120</td>
<td>1.9</td>
</tr>
<tr>
<td>Brubacher et al., 1978</td>
<td>21/M</td>
<td>150/100</td>
<td>2.1</td>
</tr>
<tr>
<td>Farfel et al., 1979</td>
<td>17/F</td>
<td>160/105</td>
<td>—</td>
</tr>
<tr>
<td>Grekin et al., 1979</td>
<td>33/M</td>
<td>200/110</td>
<td>1.7</td>
</tr>
<tr>
<td>Lee et al., 1979</td>
<td>9/F</td>
<td>120/90</td>
<td>—</td>
</tr>
<tr>
<td>Lee and Morgan, 1980</td>
<td>23/M</td>
<td>160/106</td>
<td>2.1</td>
</tr>
<tr>
<td>Schambelan et al., 1981</td>
<td>13/F</td>
<td>240/140</td>
<td>—</td>
</tr>
<tr>
<td>Sanjad et al., 1983</td>
<td>20/F</td>
<td>180/106</td>
<td>1.6</td>
</tr>
</tbody>
</table>

BP = blood pressure; GFR = glomerular filtration rate; Aldo = aldosterone; PRA = plasma renin activity; ANG I = angiotensin I; P_{ald} = plasma aldosterone; UD = undetectable. A dash indicates data not available.

*During diazide therapy.
Clinical Examination

On first admission the patient was slightly overweight (height, 156 cm; weight, 60 kg). Blood pressures of 144 to 190/110 to 125 mm Hg were obtained on several occasions, and no differences between measurements of upper and lower extremities were recorded. Results of the following blood tests were repeated.

- Blood pressure measurements of upper and lower extremities were recorded, and no differences were observed between the levels.
- Urinary cortisol (125 nM) and conventional creatinine, levels of blood glucose (4.1 mmol/L), serum creatinine (71 /uM), serum magnesium (0.75 mM), and serum creatinine kinase (84 U/L; normal < 210 U/L); daily variation of serum creatinine was noted.
- Aldosterone determinations were done using CIS-aldosterone radioimmunoassay kit (Gis-Sur-Yvette, France).
- Plasma renin activity from renal veins was measured.
- The 24-hour urinary excretion of vanillylmandelic acid (206 /uM), serum calcium (2.4 mM), fasting serum creatinine (71 /uM), and serum uric acid (16-17 /uM; normal, 8-35 /uM); and urinary excretion of amino acids and glucose.
- Chest roentgenogram, urography, renography, and renal and adrenal angiography were normal.
- Plasma potassium values were 5.2 to 6.4 mM, and plasma chloride values were 114 mM (see Table 1; Table 2). Plasma renin activity from renal veins was 0.1 to 1.0 ng of angiotensin I/ml/hr (normal, 0.9-5.0 ng angiotensin I/ml/hr).
- The 24-hour urinary excretion of aldosterone (20.2 nmol, 7.3 /uM), sodium (138 mmol), and potassium (65 mmol) were normal. The aldosterone determinations were done using CIS-aldosterone radioimmunoassay kit (Gis-Sur-Yvette, France). The phenolsulfonphthalein excretion was 44% (normal > 32%).

During the follow-up (1979-1982) the patient’s physical status remained normal. Plasma potassium level was 5.1 to 6.2 mM, and blood pressure was 130 to 180/80 to 108 mm Hg. First-degree hypertension-related changes were observed in ocular fundi vessels.

At the beginning of 1984, special attention was paid to the acid-base analysis, which showed a mild hyperchloremic acidosis: pH, 7.34 to 7.37; plasma HCO₃⁻ concentration, 20.3 to 22 mM; plasma chloride level, 111 mM; and base excess, -3.0 to -4.4 mM. The pH of urine varied between 6.0 and 7.0 (dipstick) during uncorrected acidosis. On two different occa-
sions after overnight recumbency, the plasma aldosterone level was 575 and 900 pM (20.7 and 32.4 ng/dl) and the daily urine aldosterone was 16.9 nmol (6.1 μg). The corresponding plasma renin activity was low (0.4 and 0.2 ng angiotensin I/ml/hr), and plasma potassium level was elevated (5.3 and 6.0 mM). The 4-hour upright position had no effect on plasma aldosterone level (740 and 350 pM; 26.7 and 12.6 ng/dl) or on plasma renin activity (0.6 and 0.7 ng angiotensin I/ml/hr), respectively.

Potassium excretion was not correlated with plasma level in free-living conditions (see Table 2). Serum angiotensin converting enzyme activity was 32 U/L (normal, 20–80 U/L). Fractionated bicarbonaturia was 0.96%, and potassium clearance was measured three times (5.4, 6.0, and 11.3 ml/min). The patient’s Na⁺-K⁺ pump activity and lithium countertransport of red blood cells were comparable to values found in normal subjects (Table 3).

Treatment

A search of the literature revealed that the patient’s findings were compatible with those of type II pseudohypoaldosteronism (see Table 1). Thereafter a regimen of hydrochlorothiazide (50 mg/day) was started, which normalized the blood pressure (to approximately 140/95 mm Hg), plasma potassium level (4.3–4.9 mM), plasma chloride level (104 mM), and acid-base balance. Plasma aldosterone concentration was 575 to 900 pM before therapy and 470 pM (16.9 ng/dl) during therapy. Cessation of the diuretic therapy resulted in the daily urine aldosterone was 16.9 nmol (6.1 fig).

K⁺ pump activity and lithium countertransport of red blood cells were comparable to values found in normal subjects. The corresponding plasma renin activity was low (0.4 and 0.2 ng angiotensin I/ml/hr), and plasma potassium level was elevated (5.3 and 6.0 mM). The 4-hour upright position had no effect on plasma aldosterone level (740 and 350 pM; 26.7 and 12.6 ng/dl) or on plasma renin activity (0.6 and 0.7 ng angiotensin I/ml/hr), respectively.

Hyperkalemia normally is prevented by the ability of the kidneys to excrete a normal potassium load. Our patient, however, was unable to increase the amount of potassium excreted when plasma potassium concentration was elevated (see Table 2). An association of hyperkalemia with acidosis focused our attention on type 4 renal tubular acidosis, since the pH of urine exceeded 6.0 on several occasions during acidosis. In spite of the presence of acidosis and hyperkalemia, however, the findings in our patient were not compatible with those of classical type 4 renal tubular acidosis (hyporeninemic hypoaldosteronism). Our patient had normal urinary aldosterone levels but supernormal plasma aldosterone levels and elevated plasma potassium levels. In addition, low values for potassium clearance were obtained in two out of three determinations. Taken together, these findings suggest that the patient’s kidneys were unable to excrete potassium adequately.

Thus, a diagnosis of pseudohypoaldosteronism was entertained. Classical pseudohypoaldosteronism (type I of infancy) is characterized by renal salt wasting and hypotension. A syndrome of hyperkalemia and acidosis unaccompanied by renal salt wasting and frequently associated with hypertension, as seen in our patient, has been designated type II pseudohypoaldosteronism, or Gordon’s syndrome.

In a review of the literature we found 11 reports of Gordon’s syndrome (see Table 1). The syndrome has been reported to be familial, but we could not confirm or exclude this assumption in our patient, since her sister had normal plasma potassium levels and no acidosis and we had no opportunity to study the other family members. In addition, the 11 reported patients form a somewhat heterogeneous population (see Table 1) as to the extent of acidosis, hyperkalemia, and levels of aldosterone.

Although our patient’s red blood cell Na⁺-K⁺ pump activity was unaffected by treatment and was comparable to that found in normal controls, pump activity is reportedly increased in essential, but not in secondary, hypertension. Grekin et al. have proposed that Gor-

### Table 3. The Na⁺-K⁺ Pump Activity in the Patient’s Red Blood Cells

<table>
<thead>
<tr>
<th>Na⁺-K⁺ pump activity</th>
<th>Before thiazide therapy</th>
<th>During thiazide therapy</th>
<th>Normal controls (n = 42)</th>
<th>Subjects with essential hypertension (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺-K⁺ pump-mediated rubidium uptake (nmol/10⁹ cells in 60 min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>87.6±0.7</td>
<td>98.2±0.8</td>
<td>93.7±14.4</td>
<td>98.5±13.6</td>
</tr>
<tr>
<td>Active</td>
<td>71.4±0.9</td>
<td>67.4±0.8</td>
<td>71.4±9.4</td>
<td>72.0±9.0</td>
</tr>
<tr>
<td>Maximal ouabain binding (pmol/10⁹ cells)</td>
<td>0.54±0.04</td>
<td>0.51±0.04</td>
<td>0.54±0.11</td>
<td>0.50±0.08</td>
</tr>
<tr>
<td>Lithium countertransport (nmol lithium/L red blood cells x hr)</td>
<td>0.23±0.03</td>
<td>0.28±0.04</td>
<td>0.31±0.10</td>
<td>0.25±0.11</td>
</tr>
</tbody>
</table>

Values are means ± SD.
don's syndrome represents the manifestation of a deficiency of the hypothetical chloriuretic hormone. Other workers have suggested that a defect of the distal nephron exists that increases the resorptive rate for chloride relative to sodium, which results in hyperchloremic, hyperkalemic acidosis and hypertension due to hypo-volemia. Consistent with the presence of such a chloride shunt, the administration of chloriuretic diuretics corrected the hyperkalemia and acidosis in our patient and in previously reported patients.

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