Brief Communications

Secondary Hypertension Due to a Renin-Producing Teratoma

Robert N. Pursell and Pamela M. Quinlan

Twenty cases of extrarenal renin-secreting tumors have been reported, but this is the first case of a renin-producing teratoma. The patient was a 17-year-old African American girl who presented with hypertension and hypokalemia, and who was documented to have a plasma aldosterone-to-renin activity ratio consistent with secondary aldosteronism. Computed tomography demonstrated a pelvic tumor suspicious for a teratoma. With no other apparent etiology for the secondary aldosteronism, the teratoma was suspected to be an extrarenal renin-secreting tumor. This was confirmed after surgery by pathologic evaluation, and significantly reduced requirements for antihypertensive medication and potassium supplementation. Am J Hypertens 2003;16:592–595 © 2003 American Journal of Hypertension, Ltd.

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Most cases of hypertension lack an identifiable etiology and are described as essential hypertension. Secondary hypertension may present in association with hypokalemia, as illustrated in the following case presentation. Measurements of plasma renin and aldosterone can help to delineate the various causes of hypertension and hypokalemia. Suppressed plasma renin activity (PRA) with concomitant elevations in plasma aldosterone concentration (PAC), and an elevated PAC/PRA ratio, point toward a diagnosis of primary aldosteronism. A suppressed PRA and PAC suggest more rare causes of secondary hypertension including (but not limited to) congenital adrenal hyperplasia, Cushing’s syndrome, deoxycorticosteroid-producing tumor, and Liddle’s syndrome. Conversely, an elevated PRA, an elevated PAC, and a reduced PAC/PRA ratio indicate secondary aldosteronism, including renovascular hypertension, malignant hypertension, or a renin-secreting tumor.

Among the causes of secondary aldosteronism, renovascular hypertension (RVH) is most common, but it still only occurs in 0.2% to 5.0% of the population. Another cause of secondary hypertension with a presentation similar to that of RVH (namely, elevated PRA, an elevated PAC, and a reduced PAC/PRA ratio) is the rare renin-secreting tumor. The tumor usually arises from the juxtaglomerular cells of the kidney, and only 41 such cases were reported in the mid-1990s. Less frequently, non–juxtaglomerular cell renal tumors, as well as extrarenal renin-secreting tumors have been reported. To date, 20 cases of extrarenal renin-secreting tumors have been reported, but no cases of a renin-producing teratoma causing hypertension and hypokalemia have previously been reported.

Case Presentation

A 17-year-old African American girl with a past medical history significant only for asthma and sickle cell trait was found to be mildly hypertensive during an outpatient pediatric visit. One week later, laboratory studies revealed significant hypokalemia and the patient was referred to the Emergency Department. The patient was admitted to the Nephrology service with a blood pressure (BP) of 180/120 mm Hg and a potassium level of 2.0 mmol/L. The patient denied any symptoms. The family history was significant for hypertension in both of her parents, her sister, and all of her grandparents. Additionally, the maternal history was positive for sickle cell trait.

Pertinent findings on physical examination were a BP of 180/134 mm Hg in the left arm, 180/120 mm Hg in the right arm, and 176/100 mm Hg in the right leg, with a heart rate of 80 beats/min. The patient’s respiratory rate was 12 respirations/min and her temperature was 98.6°F. Funduscopic examination demonstrated mildly blurred fundi and arterial spasm. There was no jugular venous distention. Cardiac examination revealed a regular rate and rhythm with no murmurs, rub, or gallop. The lungs were clear to auscultation. The abdomen was soft and there was no hepatosplenomegaly. No abdominal bruit was present.


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The lower extremities revealed no evidence of cyanosis or edema.

Initial laboratory testing demonstrated a hemoglobin and hematocrit of 10.8 g/dL and 33.7%, respectively. White blood cell count was 8600, blood urea nitrogen 13 mg/dL, creatinine 1.1 mg/dL, sodium 139 mmol/L, potassium 2.0 mmol/L, chloride 100 mmol/L, bicarbonate 29 mmol/L, and magnesium 2.0 mg/dL. Calcium and phosphorus were 9.8 mg/dL and 3.6 mg/dL, respectively. Urinalysis demonstrated a trace of blood and protein; however, microscopic examination was negative. A drug screen was also obtained, which was negative. An echocardiogram was normal and did not demonstrate left ventricular hypertrophy. An arteriogram was negative for renovascular disease, and renal vein renin sampling failed to reveal lateralization. Computed tomography demonstrated normal adrenal glands and noted a 7.35-cm left adnexal mass suggestive of a teratoma in the pelvic region.

Potassium was partially replaced at a serum level of 3.5 mmol/L and her 24-h excretion of potassium was 111 mmol. Studies were obtained to rule out a pheochromocytoma: vanillylmandelic acid (0.4 mg/24 h) and free catecholamines (198 µg/24 h). These studies were normal. Additional studies included 17-ketosteroids (7.8 mg/24 h), ACTH (13 pg/mL), and 17-hydroxycorticosterone (5.2 mg/24 h). All of these values were within normal limits. A 24-h urine for free cortisol was also obtained, with a result of 34.8 µg, which was normal. A 24-h urine for aldosterone was 16.8 µg, a value slightly elevated for this patient’s age. Finally, several plasma aldosterone and plasma renin levels were obtained. These studies were done in a controlled setting as an inpatient and later as an outpatient in the Short Procedure Unit. At the time that these values were taken, the patient was supine. Her potassium was normal, and she was not taking any medication that would influence either her renin or aldosterone level. Her initial values revealed a plasma renin level of 12.04 ng/mL/h, which is elevated, and a plasma aldosterone level of 104 ng/dL, which is also elevated. The PAC/PRA ratio was approximately 9.0.

In addition, the second set of values obtained revealed a renin level of 16.2 ng/mL/h and an aldosterone level of 31 ng/dL. The PAC/PRA ratio was therefore <2.0. Therefore, it should be noted that the plasma aldosterone level was done on numerous occasions under similar testing conditions. All of these values were elevated and ranged between 31 and 104 ng/dL. The lowest aldosterone level (31 ng/dL) was obtained on the day that the 24-h urine for aldosterone was completed. The urine collection result was slightly elevated for the patient’s age; however, it most likely would have been higher if it had not been done at the time that the serum plasma aldosterone level was at a lower level.

The patient was initially treated with amlodipine, labetalol and potassium supplementation. The labetalol was subsequently discontinued to avoid obscuring future testing. Subsequently her BP was controlled on 20 mg of amlodipine daily and her potassium normalized with 200 mEq of potassium supplementation daily. She was also seen by Endocrinology in consultation. It was agreed that the suspected teratoma was a possible source of the patient’s hypertension and it was subsequently removed on September, 5, 2001. The presence of a benign cystic teratoma was confirmed by pathologic examination.

Several months after the removal of the teratoma, the patient was able to reduce significantly her dose of anti-hypertensive medication and potassium supplementation. Amlodipine was reduced to 5 mg daily with optimal control. Her potassium supplementation was reduced from 200 mEq to 40 mEq daily, with satisfactory potassium control. Subsequently, Norvasc (Pfizer Inc., New York, NY) was changed to Monopril (Bristol-Myers-Squibb, Princeton, NJ) because of lower extremity edema. Currently, 1 year after her initial presentation, this patient’s BP is controlled with Monopril at a dose of 10 mg daily, and she is requiring approximately 20 mEq of potassium chloride daily. Preoperative and postoperative data for this patient are summarized in Table 1.

### Table 1. Patient data

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>Preoperative</th>
<th>2 Months Postoperative</th>
<th>8 Months Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium (mEq/L)</td>
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<td>4.0</td>
<td>4.6</td>
<td>4.0</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
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<td>130/82</td>
<td>134/82</td>
<td>138/84</td>
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<tr>
<td>Potassium supplementation</td>
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<td>200 mEq/d</td>
<td>40 mEq/d</td>
<td>20 mEq</td>
</tr>
<tr>
<td>Therapy</td>
<td>n/a</td>
<td>Norvasc 20 mg</td>
<td>Norvasc 5 mg</td>
<td>Monopril 10 mg</td>
</tr>
</tbody>
</table>

n/a = not applicable.

Discussion

Patients may present with hypertension and hypokalemia resulting from an abnormality in their renin-angiotensin-aldosterone axis. Measurement of the PAC, PRA, and PAC/PRA ratio comprises a sensitive screening test for disorders of this system. An elevated PAC and PRA and a concomitantly normal or decreased PAC/PRA ratio suggest hypertension due to secondary aldosteronism. The most common cause of secondary aldosteronism is renovascular hypertension, which relies on further testing, such as a renal arteriogram and bilateral renal vein renin sampling, for a diagnosis. If these tests are unrevealing,
then alternatives in the differential diagnoses of hypertension and hypokalemia must be considered. A renin-secreting tumor, or primary reninism, represents an uncommon form of secondary hyperaldosteronism. The diagnosis of this tumor provides an opportunity to correct a rather severe state of hypertension. Certain laboratory characteristics of a patient manifesting hypertension and hypokalemia that would suggest this diagnosis include elevated levels of the inactive precursor to renin, termed prorenin. This release of prorenin appears to occur autonomously, as the prorenin concentration has been found to be consistently low (20% to 60%) in other forms of high renin states. In fact, it has been suggested that a plasma prorenin concentration of 1000 ng/mL/h or higher is strong evidence for a renin-secreting tumor. Primary reninism also tends to present with a severe form of hypokalemia (<2.0 mmol/L), because of aldosterone-induced real potassium wasting. Some patients have hyponatremia, which is attributed to pressure natriuresis or angiotensin II-mediated natriuresis.

According to Anderson et al. in their review of 15 patients with extrarenal renin-secreting tumors, there are clinical characteristics that distinguish these individuals from those with renal-based tumors. These include a preponderance of female patients (93%) and the relatively shorter duration of symptoms (21 months). An earlier report by Korzets et al. found that these patients were relatively young to middle-aged, ranging from 9 to 56 years, with a mean age of 35 years. Based on available case descriptions to date, our patient presented with a clinical picture consistent with a renal or extrarenal tumor. She was a young (17-year-old) female individual who likely had a short duration of her hypertension in that the echocardiogram did not demonstrate left ventricular hypertrophy, despite the severity of her hypertension. An elevated PRA and PAC, and normal PAC/PRA ratio, reflected secondary aldosteronism. Her normal renal angiogram and her renal vein renin sampling that failed to lateralize ruled out renovascular hypertension. Computed tomography of the abdomen and pelvis demonstrated normal kidneys and adrenal glands, providing evidence against a renal source for the renin-secreting tumor. The fact that the renal vein renin levels did not lateralize is also supportive evidence against a renal source for a renin hypersecreting tumor. Computed tomography did demonstrate a pelvic tumor that was suspicious for a teratoma. It was hypothesized that the pelvic tumor may be an extrarenal renin-secreting tumor. The patient underwent a left oophorectomy, and the pathology report confirmed the diagnosis of a benign cystic teratoma.

Therefore, our patient presented with severe hypertension and hypokalemia. Studies define that the hypokalemia was due to renal potassium wasting. Plasma aldosterone and renin levels were both elevated, therefore suggesting that the hypertension was due to secondary hyperaldosteronism. A renovascular source was ruled out based on a negative renal arteriogram. The above findings support the fact that hypertension was secondary to primary renin secretion. There was no obvious source other than the possibility of a renin-secreting teratoma. This diagnosis was further supported by the dramatic improvement in both the BP and potassium requirement after the teratoma was removed. This patient continues to require a modest amount of antihypertensive therapy for optimal BP control. It is believed that the remaining component of her hypertension is essential in origin, which is supported by a very significant family history. At approximately 6 months in the postoperative period, Monopril was discontinued. During the next 6 weeks, systolic BP ranged between 135 and 145, with diastolic BP ranging between 90 and 95 mm Hg. During this period, her BP was monitored on two occasions in the office and on a regular basis at home by the patient. Subsequently, the Monopril was restarted at a dose of 10 mg daily and optimal BP control was achieved, with systolic and diastolic pressures being consistently <130 mm Hg and <80 mm Hg, respectively. Again, given the very significant family history of hypertension, we believed that we were dealing with mild hypertension that was essential in origin. During the 6-week period during which Monopril was stopped, her potassium supplementation was discontinued. Her serum potassium ranged between 3.5 and 3.8 mEq/L. After 6 weeks, her potassium supplementation was restarted at a dose of 20 mEq daily. It was believed that the need for potassium supplementation may have been related to a rather high sodium intake in a teenage girl. This was documented by dietary history, although her specific daily sodium intake was not quantified. It was not believed that the hypokalemia was related to persistent mineralocorticoid excess. Finally, renin and aldosterone levels were not obtained off therapy, as the patient was away at college for most of the postoperative period.

The diagnoses and reporting of extrarenal renin-secreting tumors remain rare, with only 20 other cases published. This list now includes adenocarcinomas of the adrenal glands, colon, lung, ovary, and pancreas. The diversity of histology and location and the scant number of cases create difficulty in drawing conclusions regarding these patients. The initial diagnosis is made difficult by the lack of specific presenting symptoms. Because of the severity of hypertension and the potential for curative treatment, it is important to search for a renal or extrarenal renin-secreting source in young female patients with severe hypertension and hypokalemia who demonstrate PAC, PRA, and PAC/PRA ratio values consistent with secondary aldosteronism. Subsequently, the patient should be evaluated by a renal angiogram, a renal vein renin sampling, and a prorenin-to-renin ratio. In our patient, a measurement of the prorenin-to-renin ratio may have provided evidence for the hypothesis that the teratoma served as the etiology for the secondary aldosteronism. As most reported cases of an extrarenal renin-secreting tumors involve a malignancy (rather than a benign lesion as in this...
case), it is important to make a timely diagnosis, and a plasma prorenin-to-renin ratio may expedite the process.

References