Primary Hyperaldosteronism in Childhood due to Unilateral Macronodular Hyperplasia

Case Report

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SUMMARY We present the first report of primary hyperaldosteronism in childhood due to unilateral macronodular hyperplasia. A 10-year-old white boy with severe hypertension (150/100 mm Hg), hypokalemia (1.4 mEq/liter), and suppressed plasma renin activity (PRA) (< 0.1 ng/ml/hr) demonstrated fixed PRA and aldosterone (aldo) levels that did not change with alteration of dietary sodium. The paradoxical decrease in serum aldol on assumption of upright posture suggested a tumor. Prolonged ACTH administration produced a continuous rise in blood pressure, but a transient rise in aldol. A minimal decrease in urinary aldol during dexamethasone administration was noted, excluding dexamethasone-suppressible hyperaldosteronism. Blood pressure normalized with spironolactone. Computerized transaxial tomography, iodocholesterol scanning, and adrenal venography were not diagnostic of a discrete adrenal lesion. Although hyperplasia is more common than an adenoma as a cause of hyperaldosteronism in childhood, a tumor was predicted, since adrenal vein hormone sampling with ACTH stimulation lateralized aldosterone secretion unequivocally to the left adrenal gland. However, left adrenalectomy revealed macronodular hyperplasia. Postoperatively, there was reversal of hypertension, hypokalemia, and hyperaldosteronism. Thus, in childhood, unilateral hypersecretion of aldosterone may result from nodular hyperplasia, rather than a discrete adenoma. (Hypertension 6: 75-84, 1984)

KEY WORDS • hyperaldosteronism • children • unilateral hyperplasia • hypokalemia • adrenal gland • adenoma • aldosterone • adrenalectomy • renin-angiotensin system

P RIMARY hyperaldosteronism is an extremely rare childhood disorder. To date, only 20 patients have been described.1-38 The majority of children have had bilateral hyperplasia as the etiology of their hyperaldosteronism. The major symptoms and signs include hypertension, suppressed plasma renin activity, hypokalemia, and polyuria. A substantial number of the children had evidence of ophthalmologic, cardiac, and neurologic abnormalities.

We report herein metabolic and diagnostic studies in a 10-year-old boy with primary hyperaldosteronism caused by excess aldosterone secretion due to unilateral macronodular hyperplasia. Unilateral adrenalectomy resulted in normalization of blood pressure, and reversal of hypokalemia and hyperaldosteronism. Postoperatively there was slow recovery of the renin secreting system and of the response of the glomerulosa in the remaining adrenal gland to renin-angiotensin stimulation; this excluded bilateral adrenal hyperplasia as the cause of the hyperaldosteronism.

Case Report

The patient, a 10-year-old white boy, was in excellent health until 2 months prior to evaluation when he had a generalized seizure. Blood pressure was noted to be 150/100 mm Hg. Serum chemistries revealed: Na+ 149 mEq/liter, K+ 1.4 mEq/liter, Cl 97 mEq/liter, CO2 41.4 mM, and serum aldosterone 96.2 ng/dl, with...
plasma renin activity (PRA) < 1 ng/ml/hr. The diagnosis of primary hyperaldosteronism was considered, treatment with oral potassium supplementation (120 mEq/day) was initiated, and the patient was referred to the Pediatric Clinical Research Center of The New York Hospital-Cornell Medical Center. Further evaluation was performed under protocols approved by this institution's internal review board. Informed consent was obtained from the parent and assent from the patient.

On admission to the Pediatric Clinical Research Center, the patient was alert, blood pressure was 140/92 mm Hg, height 151.1 cm (95% for age), weight 36.4 kg (75% for age), serum Na\(^+\) 141 mEq/liter, K\(^+\) 3.4 mEq/liter (with oral potassium supplementation), Cl 104 mEq/liter, CO\(_2\) 25 mM, BUN 28 mg/dl, and creatinine 0.8 mg/dl. Plasma renin activity was 0.07 ng/ml/hr, serum aldosterone 29 ng/dl, urinary aldosterone 23–33 pg/dl, and salivary Na\(^+\)/K\(^+\) 3.2/23 (normal, 16 ± 10/20 ± 5). Urinalysis demonstrated a specific gravity of 1.020 with a pH of 5. Urinary quantitative protein was 0.01–0.63 g/day with a creatinine clearance of 103 ml/min/1.73 m\(^2\). Intravenous pyelogram (IVP) and voiding cystourethrogram (VCU) were within normal limits. Abdominal sonogram and computerized transaxial tomography (CTT) did not demonstrate any adrenal masses. Electroencephalogram (EEG) was normal. Electrocardiogram (ECG) revealed a prolonged QT interval and deep S in V\(_1\). M-mode echocardiogram demonstrated increased septal wall thickness and left ventricular wall thickness.

The patient's mother had hypertension associated with normal PRA and normal serum and urinary aldosterone, which did not suppress with dexamethasone administration. Thus, the familial form of hypertension, dexamethasone-suppressible hyperaldosteronism, was excluded.

### Procedures

**Adrenal Venography and Adrenal Vein Steroid Sampling**

Adrenal venography was performed by transcutaneous femoral vein puncture with bilateral adrenal venous effluent sampling during intravenous ACTH 1–24 administration (Cortrosyn: 6 IU/hr in 40 cc D\(_5\)W/hr).

**Adrenal Scintiphotography**

Dexamethasone was given for 7 days prior to tracer injection and during the imaging period. Intravenous injection of 1 mCi \[^{131}\text{I}\] \(\beta\)-iodomethyl-19-nor-cholesterol was given, and images were obtained on Days 2, 3, 4, and 5 following injection of tracer. Potassium iodide oral solution (SSKI, 6 drops daily) was given for 14 days, beginning on the day of tracer injection to block thyroid uptake of radiiodine released from the cholesterol pool.

### Methods

All steroid analyses were performed by radioimmunoassay according to modifications of previously described methods as indicated: aldosterone,\(^{21}\) deoxycorticosterone (DOC),\(^{21}\) cortisol,\(^{23}\) corticosterone,\(^{21}\) PRA,\(^{24}\) and urinary pH 1 aldosterone.\(^{22}\)

### Periods of Study

During this study, potassium intake was maintained at approximately 140 mEq/day; regular sodium diet was calculated as 87 mEq Na\(^+\)/m\(^2\)/day, low sodium was 10 mEq Na\(^+\)/m\(^2\)/day, and high sodium was 150 mEq Na\(^+\)/m\(^2\)/day. Dexamethasone was administered in a dose of 0.5 mg orally every 6 hours. Spironolactone was administered as 12.5 mg by mouth every 12 hours.

The effect of posture on serum aldosterone levels was evaluated in blood samples obtained at 0800 hours after overnight recumbency, and again at 1200 hours after 4 hours of ambulation. Cortrosyn (1-24 ACTH) was administered as 0.6 mg/day on Day 1, and 0.4 mg/day on Days 2–5 by continuous intravenous infusion.

![Figure 1](http://hyper.ahajournals.org/)  
**Figure 1.** Preoperative metabolic, blood pressure, and hormonal responses to regular, low, and high sodium diets.
TABLE 1. Hormonal Response to Upright Posture

<table>
<thead>
<tr>
<th>Condition</th>
<th>Serum aldosterone (ng/dl)</th>
<th>Serum cortisol (μg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular sodium diet</td>
<td>flat 64.6</td>
<td>13.4</td>
</tr>
<tr>
<td></td>
<td>upright 39.8</td>
<td>6.8</td>
</tr>
<tr>
<td>Low sodium diet</td>
<td>flat 43.5</td>
<td>13.2</td>
</tr>
<tr>
<td></td>
<td>upright 39.2</td>
<td>9.3</td>
</tr>
<tr>
<td>High sodium diet</td>
<td>flat 45.1</td>
<td>10.4</td>
</tr>
<tr>
<td></td>
<td>upright 34.7</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Preoperative Examination

Metabolic and Blood Pressure Response to Alteration of Dietary Sodium Intake

In response to alteration of dietary sodium intake, the patient demonstrated a fixed and suppressed PRA and a fixed and increased urinary aldosterone excretion (Figure 1). Although the patient was normokalemic with potassium supplementation, attempts to decrease potassium intake resulted in a decrease in serum potassium levels associated with continued kaliuresis. On a low sodium diet, an increase in serum potassium associated with potassium retention occurred, while a high sodium diet resulted in a kaliuresis and a decrease in serum potassium. During the low sodium diet, the patient was able to achieve renal sodium conservation, without an increase in PRA or urinary aldosterone excretion. Blood pressure was constant throughout this study period and was above the 90th percentile for age.

Dexamethasone Administration

Dexamethasone administration did not decrease urinary aldosterone excretion or blood pressure.

Spironolactone (Aldactone RX) Administration

One week of spironolactone administration was associated with a decrease in blood pressure, although there was no increase in PRA, aldosterone excretion, or sodium diuresis, and weight loss was not observed. There was a transient increase in serum potassium associated with potassium retention, but when potassium intake was decreased, the rise in serum potassium was not sustained.

Response to Upright Posture

During regular, low, and high sodium intake, serum aldosterone varied in a circadian pattern, similar to cortisol (Table 1).

Adrenal Scintigraphy

Both adrenal glands were visualized; however, uptake by the left adrenal occurred on Day 3, while the right adrenal gland was visualized on Day 5. The early uptake on the left was suggestive of an adenoma of the left adrenal gland. However, the presence of concurrent hyperplasia on the right could not be excluded.

Adrenal Vein Steroid Sampling

The excess aldosterone secretion appeared to be localized to the left adrenal gland by adrenal vein effluent sampling (Table 2).

ACTH Administration

ACTH was administered after a 6-week period of spironolactone treatment, and 1 week after spironolactone had been discontinued. ACTH administration resulted in a marked increase in urinary aldosterone excretion.
cretion, which returned to baseline levels by the third day, despite continued ACTH infusion (Figure 2, Table 3). Except for the first day, sodium retention was not observed. The fasciculata hormones DOC and cortisol increased with continued ACTH administration. There was an increase in blood pressure. The ratio of aldosterone to DOC was 2.8 before ACTH administration and 0.29 after 6 hours of ACTH administration.

**Operation**

The patient underwent a left adrenalectomy. The left adrenal was enlarged, weighed 5 g, and measured 4 × 2.5 × 1.3 cm; multiple areas of macronodularity were observed within the cortex. Multiple cross sections (Figure 3 A) revealed a prominent distinct cortical zone that became grossly nodular at various points.

The cortical nodularities were dark yellow and ranged from 0.3 to 0.7 cm in diameter. The same pattern was identified throughout the entire gland.

Microscopic sections revealed diffuse cortical hyperplasia with multiple nodules representing focal expansions of the cortical tissue with which they were continuous (Figure 3 B). The nodules were not encapsulated, and all three cortical layers were recognized throughout. On reticulin stain, the glomerulosa and fasciculata were clearly seen (Figure 3 B and inset).

**Postoperative Care**

**Metabolic and Blood Pressure Response in the Immediate Postoperative Period and with Dietary Sodium Restriction**

Immediately after surgery, urinary aldosterone excretion decreased to undetectable levels (Figure 2). A

**Table 2. Adrenal Vein Steroid Sampling with ACTH Stimulation**

<table>
<thead>
<tr>
<th>Location</th>
<th>Aldosterone (ng/dl)</th>
<th>DOC (ng/dl)</th>
<th>Corticosterone (µg/dl)</th>
<th>Cortisol (µg/dl)</th>
<th>Aldosterone/cortisol (ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left adrenal vein</td>
<td>5795</td>
<td>16,034</td>
<td>90</td>
<td>1896</td>
<td>3</td>
</tr>
<tr>
<td>Right adrenal vein</td>
<td>107</td>
<td>4885</td>
<td>140</td>
<td>2233</td>
<td>0.05</td>
</tr>
<tr>
<td>IVC below adrenal veins</td>
<td>89</td>
<td>193</td>
<td>2.4</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>Peripheral vein</td>
<td>62</td>
<td>187</td>
<td>3.4</td>
<td>25</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3. Prolonged ACTH Test**

<table>
<thead>
<tr>
<th>Condition</th>
<th>PRA (ng/ml/hr)</th>
<th>Aldosterone (ng/dl)</th>
<th>Cortisol (µg/dl)</th>
<th>DOC (µg/dl)</th>
<th>Urine aldosterone (µg/dl)</th>
<th>Sodium (Intake/output)</th>
<th>Potassium (Intake/output)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative: 60 units Day 1, 40 units Days 2-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-ACTH</td>
<td>0.06</td>
<td>23</td>
<td>9</td>
<td>8</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 6 hours</td>
<td>0.06</td>
<td>64</td>
<td>25</td>
<td>216</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After Day 1</td>
<td>—</td>
<td>51</td>
<td>28</td>
<td>508</td>
<td>101</td>
<td>116/52</td>
<td>140/123</td>
</tr>
<tr>
<td>After Day 2</td>
<td>0.06</td>
<td>32</td>
<td>46</td>
<td>278</td>
<td>64</td>
<td>77/88</td>
<td>125/121</td>
</tr>
<tr>
<td>After Day 3</td>
<td>0.12</td>
<td>14</td>
<td>77</td>
<td>362</td>
<td>27</td>
<td>127/120</td>
<td>138/80</td>
</tr>
<tr>
<td>After Day 4</td>
<td>0.36</td>
<td>11</td>
<td>80</td>
<td>622</td>
<td>34</td>
<td>109/118</td>
<td>137/176</td>
</tr>
<tr>
<td>3½ months postoperative: 60 units Day 1, 40 units Days 2-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-ACTH</td>
<td>4.1</td>
<td>7</td>
<td>8</td>
<td>7.5</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 6 hours</td>
<td>7.3</td>
<td>22</td>
<td>39</td>
<td>214</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After Day 1</td>
<td>4.5</td>
<td>5</td>
<td>42</td>
<td>138</td>
<td>12.6</td>
<td>100/8</td>
<td>56/74</td>
</tr>
<tr>
<td>After Day 2</td>
<td>2.0</td>
<td>UD</td>
<td>46</td>
<td>106</td>
<td>3.6</td>
<td>109/6</td>
<td>57/61</td>
</tr>
<tr>
<td>After Day 3</td>
<td>0.3</td>
<td>UD</td>
<td>47</td>
<td>144</td>
<td>UD</td>
<td>99/21</td>
<td>57/53</td>
</tr>
<tr>
<td>After Day 4</td>
<td>0.3</td>
<td>UD</td>
<td>52</td>
<td>251</td>
<td>UD</td>
<td>50/29</td>
<td>47/54</td>
</tr>
<tr>
<td>After Day 5</td>
<td>0.7</td>
<td>UD</td>
<td>43</td>
<td>275</td>
<td>UD</td>
<td>114/93</td>
<td>55/70</td>
</tr>
<tr>
<td>8 months postoperative: 60 units Day 1, 40 units Days 2-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-ACTH</td>
<td>7</td>
<td>19</td>
<td>14</td>
<td>26</td>
<td>6.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 6 hours</td>
<td>2.8</td>
<td>18</td>
<td>37</td>
<td>313</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After Day 1</td>
<td>3.2</td>
<td>7</td>
<td>43</td>
<td>193</td>
<td>15.4</td>
<td>110/20</td>
<td>57/100</td>
</tr>
<tr>
<td>After Day 2</td>
<td>1.9</td>
<td>UD</td>
<td>54</td>
<td>155</td>
<td>4.0</td>
<td>111/11</td>
<td>55/63</td>
</tr>
<tr>
<td>After Day 3</td>
<td>4.1</td>
<td>UD</td>
<td>60</td>
<td>213</td>
<td>0.8</td>
<td>107/21</td>
<td>57/59</td>
</tr>
<tr>
<td>After Day 4</td>
<td>0.1</td>
<td>UD</td>
<td>52</td>
<td>226</td>
<td>UD</td>
<td>109/46</td>
<td>58/64</td>
</tr>
<tr>
<td>After Day 5</td>
<td>0.2</td>
<td>UD</td>
<td>63</td>
<td>317</td>
<td>UD</td>
<td>65/78</td>
<td>39/70</td>
</tr>
</tbody>
</table>

UD = undetectable.
marked sodium diuresis was accompanied by a 3 kg weight loss, which was observed by the second and third postoperative day. The patient demonstrated potassium retention, and there was an increase in serum potassium and a decrease in serum sodium. The PRA remained suppressed. Blood pressure decreased to within the 90th percentile for age. At 2½ weeks after adrenalectomy, the patient was unable to conserve sodium during dietary sodium restriction to 10 mEq/day. This was associated with a minimal increase in PRA (4.4 ng/ml/hr), no increase in urinary aldosterone, a decrease in serum sodium (132 mEq/liter), and a marked increase in serum potassium (5.7 mEq/liter). Also observed were a continued potassium retention and decreased weight.

**Metabolic and Blood Pressure Response**

**3½ Months Postoperatively**

The patient remained normotensive. Although the admission PRA had been suppressed, a decrease in sodium intake to 25 mEq/day resulted in increased PRA and slightly increased urinary aldosterone excretion (Figure 4, Table 3). Serum potassium was still elevated. With prolonged ACTH administration, there was a brisk increase in aldosterone excretion, decrease...
in serum potassium associated with a kaliuresis, and marked sodium retention. The blood pressure rose with ACTH stimulation. Serum cortisol levels were not significantly different from the response observed in the preoperative period. Although serum DOC levels appeared lower than in the preoperative period, they were within the ranges previously observed in normal individuals during ACTH stimulation. By the second day of ACTH administration, urinary aldosterone decreased to basal levels and then declined to undetectable levels.

With decreased sodium intake, the patient was again unable to achieve sodium conservation. Despite an increase in PRA (15 ng Al/ml/hr), urinary aldosterone did not increase significantly (<1 /u.g/12 hours). A marked increase in serum potassium (6.1 mEq/liter) accompanied by weight loss and potassium retention was observed.

Primary hyperaldosteronism is a model of mineralocorticoid hypertension. The hallmarks of the disorder classically include hypertension, suppressed PRA, and decreased serum potassium levels. In adults, the most frequently reported cause of primary hyperaldosteronism is a single adrenal adenoma, and less commonly, bilateral hyperplasia. Of note is that patients have been reported with primary hyperaldosteronism due to bilateral single adrenal adenoma, with normotension and normokalemia. In childhood, bilateral adrenal hyperplasia is the more common etiology of primary hyperaldosteronism. Our patient is most similar to the patient of Ganguly et al., a 45-year-old man in whom primary hyperaldosteronism was due to unilateral oversecretion of aldosterone due to unilateral adrenal hyperplasia.

Several techniques have been developed to aid in the definition of the cause of primary hyperaldosteronism. These include adrenal venography, isotopic adrenal scanning, aldosterone response to assumption of upright posture, adrenal vein steroid sampling, aldosterone/DOC ratios, 18-OH-corticosterone levels, response to glucocorticoid administration, and linear discriminant analysis.

In our patient, adrenal venography did not demonstrate a discrete lesion, although the left gland appeared slightly larger than the right. Further, although dexamethasone was administered in an effort to suppress the normally functioning adrenal tissue and thus decrease the uptake of radioactivity by normal tissue over the first 5 to 6 days, a definitive diagnosis could not be made based on the interpretation of the 131-I-cholesterol scan.

The anomalous decline of aldosterone in patients with an adenoma on assumption of upright posture was initially described by Ganguly et al. This observation is postulated to reflect a predominant role of ACTH in the modulation of aldosterone secretion by adrenal adenomas. However, Weinberger et al. reported that
two of eight patients with hyperplastic disease demonstrated anomalous decline in plasma aldosterone. This may reflect a lack of rise of angiotensin II. Further, recent data by Kern et al. suggested that ACTH is the dominant stimulus of episodic aldosterone secretion in patients with adrenal adenomas or hyperplasia. In addition, Wenting et al. demonstrated that ACTH dependency cannot be used as an absolute criterion for differentiating hyperaldosteronism due to adenoma formation from that due to adrenal hyperplasia.

Adrenal venous sampling is perhaps the most definitive technique used to localize an adrenal lesion. Measurement of both cortisol and aldosterone and the use of ACTH allow for verification of sample source to correct for dilution factors, and avoidance of errors due to the episodic secretion of steroids. Steroid sampling of adrenal vein effluents was performed in our patient under ACTH stimulation, and unequivocally localized excess aldosterone secretion to the left adrenal gland. Table 4 gives the adrenal vein steroid determinations in primary hyperaldosteronism described in the literature. The aldosterone/cortisol ratio in the adrenal vein of the affected/nonaffected gland has been useful in differentiating adenoma from hyperplastic disease. However, marked overlap occurs. In the child described in this report, the higher to lower ratio of aldosterone/cortisol (61:2) was slightly greater than the highest ratio recorded for patients with hyperplasia, and within the wide range recorded for adenoma formation.

Preoperatively, with prolonged ACTH administration the patient was able to produce even greater amounts of aldosterone, and although blood pressure rose, neither kaliuresis, sodium retention, nor significant change in serum electrolytes were observed, suggesting that the renal mineralocorticoid receptors were saturated and that perhaps ACTH administration caused an increase in blood pressure at the vascular level. Alternatively, the rise in blood pressure could be due to the effect of increased glucocorticoid levels on the vascular system. The decline in aldosterone excretion by the third day of ACTH administration to below baseline levels has been noted previously in primary hyperaldosteronism due either to an adenoma or hyperplasia. This pattern of response is similar to that noted in normotensive individuals.

The ratio of aldosterone to DOC in the baseline and ACTH-stimulated state has been used to differentiate primary hyperaldosteronism due to an aldosterone-producing tumor, from hyperplasia. Recently, Guthrie has shown that, in patients with adrenal adenomas, the adrenal production of hormones in the biosynthetic pathway of DOC to aldosterone are hypersensitive to physiologic amounts of ACTH. The decreased ratio in patients with adenoma argues for an intrinsic defect in the adrenal gland in the steroidogenic pathways in patients with adenoma formation. In our patient, the aldosterone/DOC ratios were consistent with those reported for patients with adenomas. Further, the adrenal vein effluent steroid sampling demonstrated marked increase in DOC as well as aldosterone production.

The cumulative results of all the studies argued for the existence of a unilateral lesion. Although biopsy of the contralateral gland was not obtained when left adrenalectomy was performed, there has been a decline in blood pressure to normal (1-year postoperative blood pressure, 106/70 mm Hg), and the hypovolemia noted in primary hyperaldosteronism postoperatively suggests the remaining adrenal gland is not hyperplastic.

The effect of excess aldosterone on the function of the surrounding adrenal in the case of hyperplasia and adenoma, or the contralateral gland in the case of adenoma, is still the subject of study. Conn et al. reported that the hypervolemia noted in primary hyperaldosteronism may result in suppression of renin secretion, and thus result in a reduction of aldosterone production from the nontumorous gland. Studies by Biglieri et al. have demonstrated that, during the first month

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**Figure 5.** Postoperative (8 months after unilateral adrenalectomy) metabolic, blood pressure, and hormonal responses to ACTH administration and dietary sodium restriction.
following adrenalectomy, the contralateral adrenal gland is not responsive to stimuli of either ACTH or angiotensin II. After the first few months, however, although baseline aldosterone levels may be depressed, the adrenal gland responds to stimuli such as hyponatremia or ACTH. It has been recommended that pretreatment with an aldosterone antagonist such as spironolactone can hasten the recovery of the juxtaglomerular apparatus. However, it is apparent that the functional recovery of the adrenal gland, despite increased PRA levels, is not improved. Further, Brown et al. have suggested that, as angiotensin II receptors are present in adjacent nontumorous tissue, the absence of appropriate response to a stimulus of angiotensin II (sodium deprivation) is consistent with a defect in the biosynthetic pathway of this tissue. In our patient, in the immediate postoperative period, despite pretreatment with spironolactone, the response of renin and aldosterone to sodium deprivation was inadequate. By 3½ months postoperatively, the juxtaglomerular apparatus appeared to be functioning normally, but the adrenal glomerulosa response to angiotensin II was still blunted. Thus, aldosterone secretion in response to ACTH was normal, while the response of the glomerulosa to secrete aldosterone under angiotensin II stimulation was impaired. At 8 months postoperatively, the adrenal glomerulosa response to angiotensin II was normal.

The effect of ACTH preoperatively as compared to the postoperative period is significant for the difference in the ability of ACTH to affect sodium retention. Preoperatively, although ACTH administration produced marked increases in urinary aldosterone, renal sodium conservation was minimal, suggesting that the patient was in renal escape. The postoperative aldosterone response to ACTH stimulation, albeit transient and of a lesser magnitude than that which we have reported in normotensive children, resulted in a
marked degree of sodium retention, kaliuresis, and a decrease in serum potassium levels. This may be due to the mineralocorticoid effect of aldosterone (or alternatively, DOC) binding to Type I renal cytosol receptors, which had been unoccupied in the postoperative period due to deficient aldosterone production from the remaining adrenal glomerulosa of the contralateral gland.

Thus, studies in this patient have demonstrated that, in childhood, unilateral secretion of aldosterone in primary hyperaldosteronism may be due to unilateral macronodular hyperplasia. Further, the contralateral adrenal gland may be refractory to the stimuli of angiotensin II, ACTH, and potassium, as has been reported in patients following unilateral adrenalectomy for adrenal adenomas. However, the ACTH response recovered more quickly. The mechanism by which hyperplasia occurs in one adrenal and not the other remains unclear.

### Acknowledgments

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