Elevated Renin and Aldosterone Levels in a Young Woman With Hypertension

Bader Kfoury and Jordana B. Cohen

Clinical Presentation

A 20-year-old woman was referred to the nephrology clinic for evaluation of resistant hypertension diagnosed at age 16 years, with blood pressures in the 140s/90s on treatment with amlodipine-valsartan-hydrochlorothiazide, 10-320-25 mg.

The patient’s medical history was otherwise significant for polycystic ovarian syndrome, for which she was receiving treatment with ethinyl estradiol/drospirenone, an oral contraceptive pill (OCP). She had previously tried a 4-month discontinuation of this OCP, but her blood pressure remained persistently elevated. She refrained from alcohol, illicit drugs, tobacco, and over-the-counter medications. Both of her parents had hypertension diagnosed in their 30s, and neither had a known secondary cause of hypertension. She had normal findings from physical examination, notable for body mass index of 20.4 kg/m², with no retinal changes, hirsutism, striae, or peripheral edema.

Laboratory testing revealed plasma renin activity (PRA) > 181.7 ng/mL/h and plasma aldosterone concentration of 215 ng/dL, confirmed on repeat testing. Other relevant laboratory values are presented in Table 1.

- What is the differential diagnosis of the elevated PRA and plasma aldosterone values?
- Is there a role for renal vein sampling in patients with this clinical presentation?
- What is the mechanism of this patient’s elevated renin level?
- How should this patient be treated?

Discussion

What is the differential diagnosis of the elevated PRA and plasma aldosterone values?

In a young patient with resistant hypertension, elevated PRA and aldosterone concentration can be seen in association with parenchymal kidney disease, fibromuscular dysplasia, small-vessel vasculitis, coarctation of the aorta, medications, and less commonly, renin-secreting tumors.

Fibromuscular dysplasia, vasculitis, and coarctation of the aorta can reduce intrarenal blood flow, as well as sodium and chloride delivery to the macula densa, all resulting in increased renin secretion from the juxtaglomerular cells and in turn, increased aldosterone release from the adrenal glomerulosa. This patient had equal blood pressure determination in each arm and a normal echocardiogram, making aortic coarctation unlikely. Computed tomography angiography and arteriography demonstrated no evidence of kidney artery stenosis (Fig 1A) or small-vessel disease in the kidneys (Fig 1B).

Is there a role for renal vein sampling in patients with this clinical presentation?

Renal vein sampling (RVS) is used to assess for laterallization in the presence of a renin-secreting tumor. The high PRA in our patient suggested the possibility of a renin-secreting tumor. There are approximately 100 cases of renin-secreting tumors described in the literature.2 Like our patient, most occur in young women with marked hypertension and elevation of PRA and aldosterone level. RVS can confirm the laterality of a renin-secreting tumor before excision and may be useful in individuals in whom a renin-secreting tumor is too small to identify on imaging.2 RVS was performed in our patient (Fig 1A), which demonstrated only modest right-sided laterallization (Table 2).

What is the mechanism of this patient’s elevated renin level?

Several medications can cause modest elevations in PRA, with resulting plasma aldosterone level increases, including angiotensin receptor blockers, dihydropyridine calcium channel blockers, diuretics, mineralocorticoid antagonists, and selective serotonin reuptake inhibitors. Unlike other synthetic progesterone components of oral contraceptives, drospirenone is derived from 17-spirolopanolactone.5 Drospirenone competes with aldosterone at the mineralocorticoid receptor, leading to a typically modest elevation in renin activity (mean increase of 2.8 ng/mL/h from baseline, maximum level of 10.8 ng/mL/h in normotensive women).
angiotensin II, and aldosterone values (mean increase of 10 ng/dL, maximum reported level of 135 ng/dL in a normotensive woman 4). To our knowledge, this magnitude of elevation in renin activity and aldosterone level has not been previously reported with drospirenone and was likely potentiated by the patient’s antihypertensive medications.

How should this patient be treated?
Spironolactone has antiandrogen effects in polycystic ovarian syndrome5 and may provide added benefit beyond its antihypertensive effects in this patient. As such, this would be a reasonable next choice for her. Other options include eplerenone or a potassium-sparing diuretic, loop diuretic, or β-blocker.

Final Diagnosis
Essential hypertension with reversible severe elevation of PRA and plasma aldosterone level due to ethinyl estradiol/drospirenone-containing oral contraceptive pill.

Table 1. Laboratory Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.58</td>
<td>0.44-1.03</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>3.6</td>
<td>3.6-5.1</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>9.7</td>
<td>8.9-10.3</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.2</td>
<td>3.5-5.5</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>91</td>
<td>70-99</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>236</td>
<td>&lt;239</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol, mg/dL</td>
<td>121</td>
<td>&lt;129</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol, mg/dL</td>
<td>87</td>
<td>40-59</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>81</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone, mIU/L</td>
<td>1.66</td>
<td>0.4-4</td>
</tr>
<tr>
<td>Renin activity, ng/mL/h</td>
<td>&gt;181.7</td>
<td>Supine: 0.2-1.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upright: 0.5-4.0</td>
</tr>
<tr>
<td>Aldosterone, ng/dL</td>
<td>215</td>
<td>Upright: 4.0-31.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Supine: ≤16.0</td>
</tr>
</tbody>
</table>

*aThe detectable upper limit of the laboratory is 181.7 ng/mL/h, so the patient’s exact renin activity level is not known.

Reference range for renin activity is for an adult with a normal sodium diet.

Table 2. Renal Vein Sampling Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renin activity, ng/mL/h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior vena cava</td>
<td>38.6</td>
<td></td>
</tr>
<tr>
<td>Right renal vein</td>
<td>52.0</td>
<td></td>
</tr>
<tr>
<td>Left renal vein</td>
<td>31.1</td>
<td></td>
</tr>
<tr>
<td>Lateralization index</td>
<td>1.7</td>
<td></td>
</tr>
</tbody>
</table>

*aLateralization index is calculated by dividing the higher renin level by the lower renin level from respective renal vein measurements. The reference range for the lateralization index is <1.55, based on previous case series.2

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Final Diagnosis
Essential hypertension with reversible severe elevation of PRA and plasma aldosterone level due to ethinyl estradiol/drospirenone-containing oral contraceptive pill.

Figure 1. Computed tomography was performed concurrently with renal vein sampling, with (A) kidney artery angiography demonstrating no evidence of kidney artery stenosis and (B) arteriography demonstrating no evidence of small-vessel disease.
Article Information

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References


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