Sixteen Years Experiences in Six Cases of Conn Syndrome in Jakarta

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ABSTRACT

Primary hyperaldosteronism or Conn syndrome is the syndrome formed from the triad of hypertension, hypokalemia, and metabolic alkalosis.

Six patients of Conn syndrome, two females (21 and 50 years) and 4 males (30, 33, 46, and 51 years), were reported. All of the cases came with the symptoms of weakness of the lower extremities in conjunction with hypertension. The plasma aldosterone level was high with the very low plasma renin activity in all of the cases. All of the patients in this case had metabolic alkalosis. Unilateral adrenal mass was found on CT-Scan or MRI imaging. Following adrenalectomy, three patients (one female and two males) still needed one type of anti hypertension drug. All of the patients did not require anti aldosterone anymore. The plasma aldosterone returned to normal value in three patients while in three other patients were not checked. The histopathology of the adrenal revealed the adenoma of the adrenal cortex in all of the six cases.

Key words: hyperaldosteronism, adrenalectomy.

INTRODUCTION

Hypertension refers to high blood pressure of more than 140/90 mmHg, as defined by the experts in The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 2003.1

Primary aldosteronism is one of the etiologies of hypertension and the prevalence is very rare, accounted less than 5% of all hypertension patients. Primary aldosteronism or Conn’s Syndrome is a syndrome clinically known for its triad, which are hypertension, hypokalemia, and metabolic alkalosis. This syndrome occurs

Kata kunci: hiperaldosteronisme, adenalektomi.
due to the unilateral adenoma or hyperplasia of the adrenal cortex.

Diagnosis is made based on the triad, ARR (Aldosterone Renin Ratio), aldosterone suppression test, and CT-scan or MRI of the adrenal gland.

The best treatment for unilateral adenoma of the adrenal is adrenalectomy by conventional surgery or laparoscopic surgery. Adrenalectomy should normalize the levels of plasma aldosterone and blood pressure without spironolactone, potassium supplementation, and antihypertensive medications.

In non-surgery treatment, the patient could consume spironolactone with maximum dose of 400 mg per day, combined with oral supplementation of potassium.

In bilateral hyperplasia of the adrenal, surgery is not the choice of treatment. Spironolactone should be given to this condition. The dosage of 12.5-25 mg per day is quite effective to control blood pressure and potassium level.

It is not rare that some patients had seen many doctors before the diagnosis is confirmed. The goal of this case-report is to remind us about how important is the triad of hypokalemia, hypertension, and metabolic alkalosis are as clinical signs in considering primary aldosteronism.

### CASE ILLUSTRATION

In sixteen years we have had experiences in handling six patients of primary aldosteronism. They were two females (21 and 50 years) and four males (30, 33, 51, and 46 years). All of them came with weakness of lower extremities in conjunction with hypertension. The potassium level were very low and all of them show the blood gas analysis of metabolic alkalosis.

The increase of plasma aldosterone level and the lowering of plasma renin activity were found in all of six patients. CT-Scan or MRI of six patients showed the unilateral enlargement of adrenal gland, in which three patients are at the left side and the other three are at the right side with the diameter around 10-37.7 mm (Figure 1).

The medications given are as follows: two patients received anti aldosterone drug and two kinds of antihypertensive drugs (HB and MK), two patients got antialdosteron and one kind of antihypertension (AS and Th), and two patients only got anti aldosteron (DE and VG). Five patients needed potassium supplementation (HB, Th, MK, VG, and DE) and only patient AS did not require potassium supplementation (Table 1).

After adrenalectomy, all patients did not require antialdosterone anymore. The plasma aldosterone of three patients (AS, HB, and DE) returned to normal level, but the other three were...

### Table 1. Baseline data of the patients before adrenalectomy

<table>
<thead>
<tr>
<th>No</th>
<th>Name</th>
<th>Age</th>
<th>First diagnosis</th>
<th>Year of operation</th>
<th>Drug</th>
<th>Aldo preop (4-31 ng/dl)</th>
<th>PRA (0,15-2,33)</th>
<th>ARR</th>
<th>CT/MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Miss. AS</td>
<td>21</td>
<td>1994</td>
<td>1996</td>
<td>Lisino 5 mg Ald 100 mg</td>
<td>&gt; norm</td>
<td></td>
<td></td>
<td>Left Adrenal Mass 14 mm</td>
</tr>
<tr>
<td>2.</td>
<td>Mr. HB</td>
<td>33</td>
<td>1995</td>
<td>1999</td>
<td>Ald 200 Lisino 10 Amlo 10 Potas 16 tab./day</td>
<td>64,97 ng/dL</td>
<td>0,07 ng/mL/jam</td>
<td>928</td>
<td>Right Adrenal Mass 15 mm</td>
</tr>
<tr>
<td>3.</td>
<td>Mr. Th</td>
<td>51</td>
<td>2000</td>
<td>2000</td>
<td>Ald 100 Amlo 10 Potas 6 tab/day</td>
<td>219 ng/dL</td>
<td>0 ng/mL/jam</td>
<td>~</td>
<td>Right Adrenal Mass 10 mm</td>
</tr>
<tr>
<td>4.</td>
<td>Mr. MK</td>
<td>46</td>
<td>2002</td>
<td>2002</td>
<td>Ald 200 Amlo 5 Lisino 10 Potas 12</td>
<td>236,9 ng/dL</td>
<td>1,46 ng/mL/jam</td>
<td>162</td>
<td>Left Adrenal Mass 97,7 mm</td>
</tr>
<tr>
<td>5.</td>
<td>Mr. VG</td>
<td>30</td>
<td>2008</td>
<td>2009</td>
<td>Ald 200 Potas 6 tab/day</td>
<td>41 ng/dL</td>
<td>0,05 ng/mL/jam</td>
<td>820</td>
<td>Left Adrenal Mass 12 mm</td>
</tr>
<tr>
<td>6.</td>
<td>Mrs. DE</td>
<td>50</td>
<td>2010</td>
<td>2010</td>
<td>Ald 100 Potas 2 tab/day</td>
<td>40 ng/dL</td>
<td>0,21 ng/mL/jam</td>
<td>190</td>
<td>Right Adr. Mass 20 mm</td>
</tr>
</tbody>
</table>

Note: Lisino = Lisinopril; Amlo = Amlodipin; Ald = Anti Aldosterone; Potas = Potassium.
not tested. During the follow up, potassium level was normal constantly without any complaints of weakness of lower extremities (Table 2). After adrenalectomy, there was no need of special care for the patients during inpatient period.

The blood pressure of three patients were normal without any antihypertensive drugs (AS, Th, and VG), but the other three (HB, MK, and DE) needed one kind of anti hypertensive medications.

The histopathology reports of all six patients were consistent for adenoma of adrenal cortex (Table 2).

DISCUSSION

Primary aldosteronism belongs to the hypertension group called “mineralocorticoid hypertension”, due to hyperactivity of the mineralocorticoid. Almost all of these hypertension group patients have normal level of plasma potassium. There was one study reported that more than 50% of patients with primary aldosteronism had normal plasma potassium level. The potassium levels of all six patients in our cases were low and all of them had the triad that led to the suspicion of Conn’s syndrome. Elevation of the aldosterone levels will stimulate the addition of sodium channel opening in the principal cell of cortical collecting duct, resulting in the increased reabsorption of sodium-ion. In line with this, the luminal part of the duct will become more negatively charged, leading to the excretion of intra cell potassium through potassium channel into the lumen of cortical collecting duct. Increase in potassium excretion is also triggered by the high flow of fluids towards the distal nephron. Both of these conditions will then lower the plasma potassium of the patient and become hypokalemia. The hypokalemic state will stimulate increased excretion of H-ion through Na-H antiporter, leading to the increased bicarbonate reabsorption in proximal tubule, which will cause the patients to suffer from metabolic alkalosis. Hypokalemia in conjunction with hyperaldosteronism will also stimulate H-K-ATPase and H-ATPase pumps in the distal nephron, which will cause the increasing of H-ion excretion and maintain alkalotic states of the patient. The plasma renin activity in patient with primary aldosteronism is very low. The hypervolemic states caused by the increasing of sodium reabsorption will suppress the renin production, lowering plasma renin activity. Hypertension in primary aldosteronism is mostly due to persistent hypervolemia.

CT-Scan and MRI of adrenal gland could show the enlargement of this gland unilaterally or bilaterally more than 1 cm. Enlargement of adrenal gland of more than 5 cm is significantly specific for the carcinoma of adrenal gland. CT-scan or MRI in all 6 patients revealed unilateral enlargement of adrenal gland with the size of less than 5 cm and the histopathology reports were consistent for adenoma of adrenal cortex.

Table 2. The data of the patients after adrenalectomy

<table>
<thead>
<tr>
<th>No</th>
<th>Name</th>
<th>Aldost (4-31 ng/dl)</th>
<th>Histopat</th>
<th>Drug</th>
<th>Blood press</th>
<th>Plasma Potas. (meq/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Miss. AS</td>
<td>19</td>
<td>Adenoma</td>
<td>--</td>
<td>120/80</td>
<td>4,2</td>
</tr>
<tr>
<td>2.</td>
<td>Mr. HB</td>
<td>5,23</td>
<td>Adenoma</td>
<td>Lisino. 5</td>
<td>140/90</td>
<td>3,54</td>
</tr>
<tr>
<td>3.</td>
<td>Mr.Th</td>
<td>--</td>
<td>Adenoma</td>
<td>--</td>
<td>130/80</td>
<td>3,9</td>
</tr>
<tr>
<td>4.</td>
<td>Mr.MK</td>
<td>--</td>
<td>Adenoma</td>
<td>Amlo.10</td>
<td>130/90</td>
<td>4,0</td>
</tr>
<tr>
<td>5.</td>
<td>Mr. VG</td>
<td>--</td>
<td>Adenoma</td>
<td>--</td>
<td>130/80</td>
<td>4,0</td>
</tr>
<tr>
<td>6.</td>
<td>Ms. DE</td>
<td>21</td>
<td>Adenoma</td>
<td>Amlo. 5</td>
<td>130/80</td>
<td>4,0</td>
</tr>
</tbody>
</table>

Note: Lisino = Lisinopril; Amlo = Amlodipin
In patient VG (Table 1), he initially came with the sign and symptom of hyperthyroidism with hypokalemia. At this time patient VG was given the treatment as hyperthyroid patient. After clinical condition of hyperthyroid has been controlled, surprisingly the level of plasma potassium was still lower than normal. With high blood pressure condition, this patient was suspected for having primary aldosteronism. Further examinations proved that the patient was suffering from primary aldosteronism.

Three out of six patients still needed one kind of anti-hypertensive medication. From the report of other investigators, around 40-60% of the patients still required antihypertensive drugs after adrenalectomy. The normalization of blood pressure depends on adenoma classification, the response to anti aldosterone before adrenalectomy, the age less than 44 years, and high blood preasure of less than 5 years. Besides these, the role of nephrosclerosis and left ventricular hypertrophy is important for the persistency of high blood pressure after adrenalectomy.5,6 Patient HB had mild renal insufficiency before adrenalectomy and he still needed one kind of anti hypertension. It is possible that he had nephrosclerosis, as was reported by Horita et al.6 It was four years after the diagnosis that patient HB finally decided to undergo adrenalectomy.

The histopathology reports of all six patients were consistent for adenoma of adrenal cortex; it means that the triad of hypertension, hypokalemia, and metabolic alkalosis in all of our six cases are valuable clinical sign in considering primary aldosteronism. Besides this, the mean ARR of the six patients is more than 200 and significant enough for the diagnosis of primary aldosteronism (Table 1). The plasma aldosterone-renin ratio or ARR has a significant diagnostic value. The ratio of more than 100 possesses high diagnostic value of the primary aldosteronism. The combination between plasma aldosterone level of 20 ng/dL (555 pmol/L) with the ARR of more than 30 have the specificity and sensitivity of 90%.7 The high ratio of ARR alone cannot ensure the diagnosis of primary aldosteronism, but it has to be combined with other test such as aldosterone suppression test. This test is done by giving NaCl orally or parenteral infusion of isotonic saline to determine whether the increasing of the aldosterone is primarily from the adrenal.8 Aldosterone suppression test was not done in all of our six cases. However, the triad of hypertension, hypokalemia, and metabolic acidosis in conjunction with the ARR more than 100 without aldosterone suppression test still possesses high diagnostic value of the primary aldosteronism in our six cases.

CONCLUSION

The triad of hypokalemia, hypertension, and metabolic alkalosis are important clinical signs in considering the primary aldosteronism. The diagnostic and management capability of primary aldosteronism in Indonesia is adequate. Adrenalectomy is good choice of treatment, without any significant difficulties.

REFERENCES