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The Usefulness of Plasma Aldosterone Concentration / Plasma Renin Activity Ratio for the Diagnosis of Aldosterone-Producing Adenoma

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Abstract Aldosterone-producing adenoma is a rare but surgically curable disease of primary aldosteronism. We experienced two cases of aldosterone-producing adenoma; the first patient was a 39-year-old woman with hypertension, and the second patient a 47-year-old woman complained of paresthesia. In both patients, the plasma aldosterone concentration / plasma renin activity ratio was inappropriately increased. The ratio is considered to be an useful screening index to predict the existence of aldosterone-producing adenoma.

Key words : Aldosterone-producing adenoma, Case report.

Introduction

Aldosterone-producing adenoma (APA) is a subtype of primary aldosteronism. Primary aldosteronism is a rare type of secondary hypertension characterized by hypokalemia, elevated plasma aldosterone concentration (PAC) and decreased plasma renin activity (PRA), however, in clinical setting the diagnostic approach to APA using plasma examination is still sometimes difficult. We present two cases of APA, in which PAC / PRA ratio was an useful screening value for the diagnosis of APA.

Case Reports

Case 1

A 39-year-old woman visited Yamato General Hospital because of further examina-

tion of hypertension. The patient had no symptoms, and no familial history of hypertension. She had been in excellent health until one year earlier, when she was diagnosed as hypertension. Her only treatment was dietary salt restriction. The physical examination was completely normal except for elevated both systolic and diastolic blood pressures of 172/106mmHg. Blood chemistries including thyroid hormones were within normal ranges except for low potassium level of 2.6mEq/l (Table 1). Further laboratory examinations revealed decreased PRA of 0.1 ng/ml/hr (normal range : 0.3-2.9ng/ml/hr), and elevated PAC of 460pg/ml (normal range : 30-159pg/ml); calculated PAC/PRA ratio was inappropriately increased to 4600, suspecting APA in our outpatient clinic.

Table 1. Laboratory Data in Case 1

Variable	Value (Normal Range)
RBC	423x10 ⁴ /μl (400-500)
Hb	12.8g/dl (12-16)
Ht	37.4% (37-47)
WBC	4950/μl (4000-10000)
PLT	31.0x10 ⁴ /μl (15-40)
TP	7.5g/dl (6.2-8.2)
Glu	88mg/dl (70-105)
T-Bil	0.5mg/dl (0.3-1.0)
GOT	14 IU/l (10-39)
GPT	11 IU/l (8-35)
LDH	341 IU/l (222-445)
T-Cho	191mg/dl (130-230)
Cre	0.8mg/dl (0.6-1.5)
CRP	<0.25mg/dl (<0.25)
Na	143mEq/l (136-148)
K	2.6mEq/l (3.6-5.0)
Cl	102mEq/l (98-108)
T-Ca	4.4mEq/l (4.2-5.2)
TSH	2.5μU/ml (0.34-3.5)
Free-T ₄	1.4ng/dl (0.97-1.79)
PAC	460pg/ml (30-159)
PRA	0.1ng/ml/hr (0.3-2.9)
Cortisol	6.6μg/dl (4.0-18.3)
17-KS	9.4mg/day (2.4-11.0)
17-OHCS	8.3mg/day (2.2-7.3)
HANP	120pg/ml (<40)

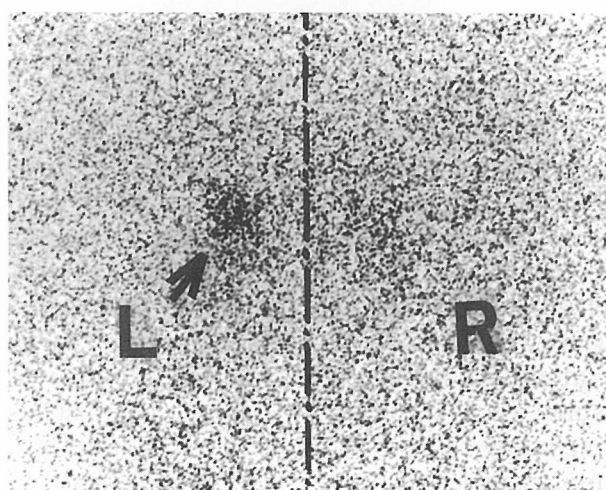


Fig. 1. Posterior adrenal scintigraphic image from case 1 at seven days after ¹³¹I-iodocholesterol administration during dexamethasone suppression, showing the radioisotope activity of the left adrenal gland (arrow) without discernible right adrenal activity. L : left, R : right adrenal gland.

Abdominal CT scanning disclosed a 15×20 mm left adrenal mass. Adrenal scintigraphy during dexamethasone suppression showed high accumulation at the left adrenal gland (Fig. 1). Pre-operative diagnosis was APA of the left adrenal gland. A laparoscopic adrenalectomy was performed at Tokuyama Central Hospital. The entire tumor weighed 3.1 gram, and showing golden-yellow on the cut-surface. The diagnosis as APA was confirmed histopathologically. Her blood pressure became normal after the removal of the tumor.

Case 2

A 47-year-old woman was admitted to Hikari City Hospital because of paresthesia of bilateral hands. The pulse rate was 102 bpm, and the blood pressure was 174/102 mmHg. There was no abnormality of general physical examination. On neurological examination, the paresthesias of the bilateral hands were noted. The results of the laboratory data showed low potassium level of 2.7 mEq/l (Table 2) and metabolic alkalosis (PaO₂ 88.1mmHg, PaCO₂ 37.1mmHg, HCO₃

Table 2. Laboratory Data in Case 2

Variable	Value (Normal Range)
RBC	404x10 ⁴ /μl (400-450)
Hb	12.1g/dl (12-16)
Ht	35.2% (37-47)
WBC	5700/μl (4000-10000)
PLT	19.5x10 ⁴ /μl (15-40)
TP	6.8g/dl (6.5-8.3)
Glu	92mg/dl (70-110)
T-Bil	1.2mg/dl (0.2-1.0)
GOT	22 IU/l (11-35)
GPT	7 IU/l (9-42)
LDH	377 IU/l (180-460)
T-Cho	237mg/dl (130-250)
Cre	0.6mg/dl (0.4-1.2)
CRP	<0.25mg/dl (<0.25)
Na	142mEq/l (136-148)
K	2.7mEq/l (3.6-5.0)
Cl	102mEq/l (98-105)
T-Ca	8.2mg/dl (8.4-10.2)
PAC	310pg/ml (30-159)
PRA	<0.1ng/ml/hr (0.3-2.9)
Cortisol	13.2μg/dl (4.0-18.3)
17-KS	6.1mg/day (2.4-11.0)
17-OHCS	4.4mg/day (2.2-7.3)

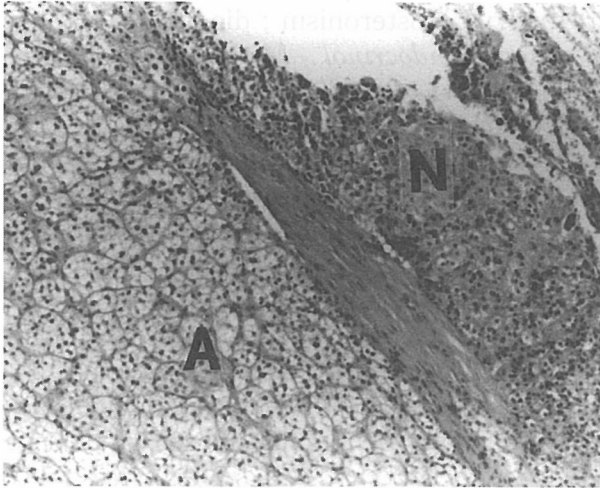


Fig. 2. Histopathological appearance of the aldosterone-producing adenoma from case 2. The adenoma cells (A) show large and clear cytoplasm, and resemble normal zona fasciculosa cells (N). HE-stain. x 20.

30.6 mmol, pH 7.52). Her symptom subsided after the supplementation of potassium and the administration of nifedipine. Laboratory examination revealed decreased PRA of <0.1 ng/ml/hr and increased PAC of 310 pg/ml; APA was suspected since PAC / PRA ratio was extremely high.

CT scanning showed a 7mm nodular lesion on the left kidney. Selective blood sampling for aldosterone determination was performed, and PAC from the left renal vein and that from the right renal vein were >4000 pg/ml and 260pg/ml, respectively. The patient was diagnosed as APA of the left adrenal gland. She underwent laparoscopic adrenalectomy. The diagnosis of adenoma was histopathologically documented (Fig. 2). The patient became normotensive and normokalemia after the operation.

Discussion

Primary aldosteronism was described in 1955 by Conn in conjunction with APA (1). Primary aldosteronism results from the renin-independent over-production of aldosterone. This syndrome is characterized by hypertension, potassium loss, and suppression of the renin-angiotensin system. Primary aldosteronism represents approximate-

ly 0.05% to 2.2% of all cases of unselected hypertension (2). At least, four types of primary aldosteronism have been described: APA, idiopathic hyperaldosteronism, aldosterone-producing adenocarcinoma, and glucocorticoid-suppressible hyperaldosteronism. Over 60% of primary aldosteronism are due to APA, and approximately 35% idiopathic hyperaldosteronism (2). The therapeutic strategy of this syndrome is dictated by the subtype; patients with APA are surgically curable, whereas those with idiopathic hyperaldosteronism are best treated with spironolactone.

The clinical features of APA are non-specific. Case 1 had moderate hypertension of one-year duration without symptoms, and case 2 complained of paresthesia probably due to hypokalemia and metabolic alkalosis. When hypertension and hypokalemia co-exist, the presence of elevated PAC and decreased PRA might make the diagnosis more likely, however, this syndrome is frequently overlooked. For instance, PRA is decreased in patients with so-called low-renin essential hypertension, and hypokalemia is observed when potassium-wasting diuretics are used.

A number of hormonal studies, pharmacologic examinations and imaging techniques have been done for the diagnosis of APA because no single test or imaging has proved to be 100% accurate. The most appropriate and cost-effective diagnostic approach to APA have been needed.

Although the ratio of PAC (pg/ml)/PRA (ng/ml/hr) greater than 250 (2) or 300 (3) have been suggestive of primary aldosteronism, there are few reports on the PAC/PRA ratio in APA. Hisamatsu et al reported that, in patients with APA, the PAC/PRA ratio was increased to more than 400 in the outpatient clinic, and suggested that the PAC/PRA ratio should be an useful screening index for the diagnostic approach to APA among hypertensive patients (4). In our patients, the ratio was inappropriately increased, which lead us the prediction of APA. The ratio might be an useful screening index, and the assessment of this ratio could avoid diagnostic delay or unnecessary test for the differential diagnosis of secondary hyperten-

sion.

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