A CASE OF ADRENOCORTICAL ADENOMA PRODUCING 11-DEOXYCORTICOSTERONE (DOC) INDEPENDENT OF ACTH CONTROL.

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Abstract : A 31-year-old woman with left adrenocortical adenoma had hypertension, hypokalemia and low plasma renin activity (PRA) level. The plasma aldosterone and urinary 17-OHCS levels were within normal range. However, the plasma 11-deoxycorticosterone (DOC) level was elevated. Diurnal variation of DOC was absent. Dexamethasone administration suppressed ACTH and cortisol levels, but did not depress DOC level. Acute synthetic ACTH administration increased cortisol level, however, DOC level was unchanged. After removal of the tumor, her blood pressure, serum potassium, PRA and DOC levels were normalized. The high level of DOC caused an increase in blood pressure and was independent of ACTH control.

Key words : Hypertension, Hypokalemia, Plasma renin activity, ACTH control
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INTRODUCTION

Excessive production of mineralocorticoid hormone, generally due to an overproduction of aldosterone, causes hypertension and hypokalemia. 11-deoxycorticosterone (DOC), a precursor of corticosterone and aldosterone, has a weak mineralocorticoid action, but its overproduction can cause hypermineralocorticism in the absence of excessive production of aldosterone or cortisol^{1~3)}. DOC secretion from an adrenocortical tumor^{2,3)} are controlled by ACTH. We report here on a case of adrenocortical adenoma producing DOC without ACTH control.

CASE REPORT

A 31-year-old woman went through her second pregnancy and delivery in May. During her second pregnancy, her blood pressure ranged between 140/80 and 150/90mmHg. She was admitted to our hospital in July, because of hypertension. Her blood pressure was 172/104mmHg and pulse rate, 74 beats per minute. Other physical examination results were negative.

Laboratory data were as follows: electrocardiogram showed U waves. The serum sodium level was 141mEq/l; potassium, 1.9mEq/l and chloride, 99mEq/l. The arterial pH showed slight alkalosis (pH 7.464) and base excess, +6.6mEq/l. All of other chemical analyses were normal. Results of hormonal studies are summarized in Table 1 and 2. Basal plasma renin activity (PRA) was low, but blood levels of adrenocorticotrophic hormone (ACTH), cortisol, progesterone, corticosterone, aldosterone and urinary excretion of 17-OHCS, 17-KS and catecholamine (such as urinary metanephrine) levels were within normal range. In contrast, DOC was remarkably high (Table 1). PRA failed to respond to 2 hour-upright posture after an intravenous administration of 40mg furosemide. Plasma levels of aldosterone and DOC were also almost unchanged (Table 2a). Plasma ACTH and cortisol levels showed daily fluctuation, but its fluctuation was not found in DOC levels. An administration of 1 mg dexamethasone at 2300 h decreased plasma levels of ACTH and cortisol at 0600 h the next day, but, plasma level of DOC was unchanged (Table 2b).

Table 1 Laboratory data

Date	7/26	8/12	9/10	11/28	
Blood pressure (mmHg)	172/104	160/100	132/78	132/80	
Serum					<normal range>
Na (mEq/l)	141	141	140	139	135-147
K (mEq/l)	1.9	2.2	4.1	3.9	3.6-5.0
Cl (mEq/l)	99	102	103	101	98-108
Plasma					
Renin activity (ng/ml/hr)	0.1	0.1	0.2	1.0	0.3-2.9
ACTH (pg/ml)	32	31	27	32	6-36
Cortisol (μ g/dl)	14.2	13.8	12.3	11.8	3.0-15.2
Progesterone (ng/ml)	1.22	1.18	1.05	1.10	0.5-1.52
DOC (ng/ml)	1.64	1.68	0.29	0.26	0.03-0.33
Corticosterone (ng/ml)	3.99	4.01	3.07	2.89	0.21-8.48
Aldosterone (pg/ml)	62	58	35	54	35.7-240
Urine					
17-OHCS (mg/day)	5.2	5.1			1.9-6.1
17-KS (mg/day)	3.6	3.4			3.1-8.8
Metanephrine (mg/day)	0.11				0.01-0.3
Normetanephrine (mg/day)	0.19				0.05-0.4

ACTH: adrenocorticotrophic hormone, DOC: 11-deoxycorticosterone

Table 2a Effects of administration of furosemide and 2 hour-upright posture

Plasma	Before	2 hour-upright
Renin activity (ng/ml/hr)	0.1	0.1
Aldosterone (pg/ml)	68	61
DOC (ng/ml)	1.63	1.62

Table 2b Daily profile and effects of administration of dexamethasone

1mg of dexamethasone (2300h)				
Plasma	06:00h	12:00h	18:00h	↓ 06:00h
ACTH (pg/ml)	32	20	15	6
Cortisol (μ g/dl)	14.1	7.6	6.3	1
DOC (ng/ml)	1.65	1.62	1.58	1.60

Table 2c Effects of acute administration of synthetic ACTH

Plasma	0min	30mins	60mins
Cortisol (μ g/dl)	14.1	28.9	29.8
Aldosterone (pg/ml)	67	95	101
DOC (ng/ml)	1.64	1.65	1.64

Table 2d Sampling data

- 1) inferior vena cava (Th12)
- 2) inferior vena cava (bifurcation)
- 3) right adrenal vein
- 4) right renal vein
- 5) left renal vein
- 6) left adrenal vein

	Cortisol(μ g/dl)	DOC(ng/ml)	Aldosterone(pg/ml)
1)	11.1	2.35	68
2)	12.5	1.60	64
3)	13.1	0.67	69
4)	15.0	2.16	64
5)	13.4	4.22	68
6)	14.0	220.00	69

Fig. 1. Computed tomography revealed a round mass in the left adrenal region.

Acute synthetic ACTH (Cortrosyn Z; 0.25mg) administration increased cortisol and aldosterone levels, but did not increase DOC levels (Table 2c). ACTH was measured by the IRMA method, cortisol by fluorescence polarization immunoassay, PRA, progesterone, corticosterone, aldosterone or DOC by the RIA method and urinary catecholamine by the HPLC method. Although adrenal scintiscanning using ^{123}I adosterol showed normal uptake, an abdominal computed tomography revealed a round mass in the left adrenal region (Fig. 1). Plasma DOC of the left adrenal vein was markedly elevated (220.00ng/ml). Plasma levels of cortisol and aldosterone were almost

Fig. 2. The left adrenal tumor, encapsulated, consisted mainly of clear cells without cellular atypia in the adrenal cortex (Hematoxylin-Eosin $\times 100$).

unchanged in those sampling blood (Table 2d). Based on these findings, a left adrenal tumor producing DOC was suggested. Oral administration of spironolactone (150mg, t.d.s. for 10 days) did not affect serum potassium level, urinary excretion of potassium level or blood pressure. After that, the left adrenal tumor ($11 \times 9 \times 8$ mm) was removed. Histologically, the encapsulated tumor consisted mainly of clear cells without cellular atypia in the adrenal cortex, a finding compatible to adrenocortical adenoma (Fig. 2). Her blood pressure, serum potassium, basal PRA and plasma DOC levels became normal after the operation.

DISCUSSION

The patient had clinical manifestation featured by hypertension, persistent hypokalemia and low level of PRA. PRA remained low following the stimulation of intravenous furosemide and 2 hour-upright position. Suppression of the renin system is a characteristic of mineralocorticoid excess¹⁻³). However, all levels of plasma aldosterone, corticosterone, cortisol and urinary excretion of 17-KS and 17-OHCS were within normal range. These clinical and laboratory findings could exclude primary aldosteronism, Cushing's syndrome and adrenogenital syndrome. After removal of the left adrenal tumor, her blood pressure, serum potassium, PRA and plasma DOC levels were normalized. She had a DOC producing adrenocortical adenoma, although we failed to measure the DOC level in tumor tissue. The increment of DOC may produce the pathological state of mineralocorticoid excess, with hypertension, hypokalemia and suppression of PRA. Plasma ACTH and cortisol levels showed daily fluctuation and were inhibited with administration of dexamethasone. Acute synthetic ACTH administration increased the cortisol level, but did not increase the

DOC level. Although aldosterone secretion in patients with primary aldosteronism^{4,5}) and DOC secretion from an adrenocortical tumor^{2,3}) are controlled by ACTH, the DOC level showed independent secretion of ACTH control in our adrenocortical adenoma. Low response of the DOC level by administration of dexamethasone or synthetic ACTH has been shown in adrenocortical carcinoma^{6,7}). Cortisol or aldosterone levels are barely responded to synthetic ACTH in those cases, although the levels increased in our case. Oral administration of 150mg spironolactone could not satisfactorily control serum potassium level, urinary excretion of potassium level or blood pressure in the patient, although such easy control has been previously reported by other investigators⁸). It has been assumed that the DOC producing adrenocortical adenoma in the patient is more autonomous than previously reported case^{2,3,8}).

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