A case of subclinical primary aldosteronism and subclinical Cushing's syndrome without risk factors of cardiovascular disease

Natsumi Kitajima[1], Toshiro Seki[1], Atsushi Yasuda[1], Masami Seki[2], Masayuki Oki[1], Atsushi Takagi[1], Masafumi Fukagawa[1]
Tokai University School of Medicine[1], Seirei Numazu Hospital[2]

【Case report】

A 49-year-old woman was referred to our hospital for the evaluation of adrenal incidentaloma. She had no past medical history and no family history of notable illness. The patient was 152.5cm tall and weighed 58.0 kg. Her blood pressure was 103/60 mmHg. She had no Cushingoid features. Osteoporosis was absent.

Urinalysis		Blood chemistry	
color	yellow	CRP	< 0.09 mg/dL [< 0.3]
pH	7.0	TP	6.9 g/dL [6.5-8.0]
protein	(-)	Alb	3.9 g/dL [3.9-4.8]
occult blood	(-)	AST	12 IU/L [< 30]
glucose	(-)	ALT	9 IU/L [< 35]
ketone body	(-)	LDH	136 IU/L [110-219]
		ALP	135 IU/L [100-310]
Hematological examination		γ-GTP	12 IU/L [< 35]
WBC	7500/μL [400-8000]	Na	141 mEq/L [136-145]
Neu	61.1% [40-70]	K	4.0 mEq/L [3.5-4.8]
Lym	29.7% [20-40]	Cl	108 mEq/L [98-108]
Mo	3.6% [3-8]	Ca	8.8 mg/dL [8.6-10.0]
Eo	4.9% [1-4]	P	3.2 mg/dL [2.5-4.5]
Ba	0.7% [0-1]	BUN	10 mg/dL [8-20]
RBC	409×10^4/μL [380-480]	Cr	0.53 mg/dL [0.5-0.8]
Hb	12.6 g/dL [11.5-15.5]	UA	3.7 mg/dL [3.0-6.0]
Ht	38.8% [34.0-42.0]	TG	51 mg/dL [50-150]
Plts	25.0×10^4/μL [14.0-40.0]	T-cho	157 mg/dL [140-220]
		HDL-cho	51 mg/dL [40-100]
		LDL-cho	97 mg/dL [< 120]
		Glucose	87 mg/dL [70-110]
		HbA1c	4.9% [4.3-5.8]

Abbreviations: [ ], reference range.

Routine laboratory examinations were within the normal ranges including normokalemia.

The circadian variation

Time	8am	11pm
Cortisol (mg/dL)	11.7	3.3
ACTH (pg/mL)	< 2.0	11.3

The overnight dexamethasone suppression test

Dxa	1mg	8mg
Cortisol (mg/dL)	1.8	1.7
ACTH (pg/mL)	< 2.0	< 2.0

The hormonal examination revealed normal circadian variation in serum cortisol levels (11.7 g/dL at 8 am and 3.3 g/dL at 11 pm) and plasma ACTH level was undetectable (< 2.0 pg/mL). Plasma cortisol level was suppressed after the low-dose overnight dexamethasone suppression test but was not suppressed after the high-dose test.

Captopril test

Time (min)	0	60	90
PAC (pg/mL)	90.7	76.1	84.7
PRA (ng/mL/hr)	2.5	0.4	0.2
ARR	36.3	190.3	423.5

Furosemide-upright test

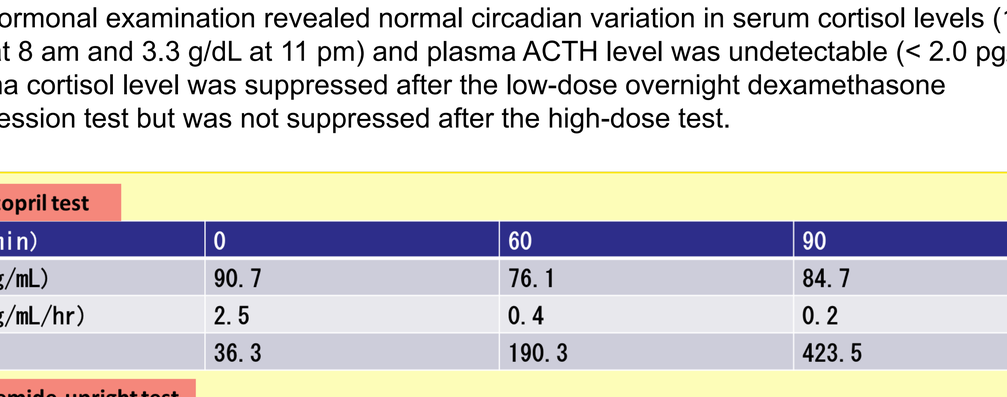
Time (min)	0	120
PAC (pg/mL)	61.6	166
PRA (ng/mL/hr)	<0.1	0.3

Saline-loading test

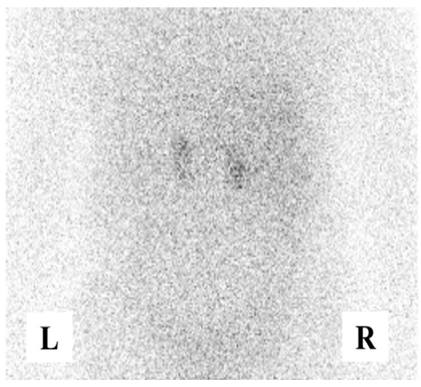
Time (min)	0	240
PAC (pg/mL)	44.4	35.3
PRA (ng/mL/hr)	0.5	0.3

The plasma aldosterone concentration (PAC) level was normal (110 pg/mL) and the plasma renin activity (PRA) was suppressed (0.1 ng/mL/hr).
The captopril test and furosemide-upright test were positive, whereas the saline-loading test was negative.

【CT scan】



CT scans of the abdomen showed bilateral adrenal tumors.



Adrenal scintigraphy revealed bilateral adrenal activity.

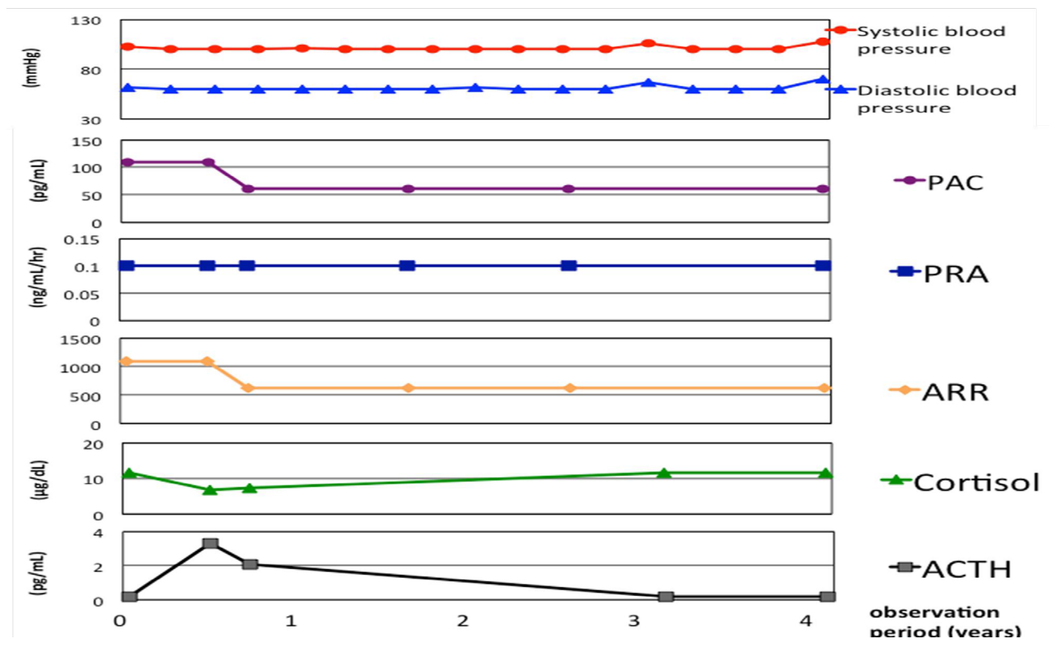
	Cortisol (μg/dL)		Aldosterone (pg/mL)	
	RAV	LAV	RAV	LAV
Baseline	20.8	25.8	3550	1570
After ACTH 250 μg	1102	894.0	27600	28600

Abbreviations: RAV, right adrenal vein; LAV, left adrenal vein; ACTH, adrenocorticotropic hormone.

To determine the laterality of the excessive cortisol or aldosterone secretion, we performed adrenal venous sampling (AVS).

Finally, we made a diagnosis of subclinical primary aldosteronism (PA) caused by both adrenal glands and subclinical Cushing's syndrome (CS) caused by both adrenal tumors.

【Clinical course】



Interestingly, this patient had no risk factors for cardiovascular disease such as hypertension, obesity, diabetes mellitus or dyslipidemia. Thus, we are observing her without medical therapy. Four years after diagnosis, she has not been detected hypertension, hypokalemia, cardiomegaly in echocardiography and atherosclerosis in carotid ultrasonography.

【Discussion】

- Patients with subclinical CS lack specific symptoms of CS but chronic exposure to subtle cortisol excess may be associated with risk factors for cardiovascular disease including diabetes mellitus, hypertension, or dyslipidemia.

- The critical issue is why excessive aldosterone secretion did not affect the cardiovascular status of this patient. In this regard, Ito et al. recently reviewed several possible mechanisms of normotensive PA (termed subclinical PA) [Ito Y, Takeda R, Takeda Y. Subclinical primary aldosteronism. Best Pract Res Clin Endocrinol Metab. 2012; 26: 485-495.]. They demonstrated that five possibilities could explain the causes of this normotensive form of PA: (a) an early state of the disease, (b) a mild form of the disease, (c) a low spontaneous baseline blood pressure level, (d) low sodium intake and/or high consumption of green tea, or (e) a low body mass index (BMI).

- Factors (a) and (b) do not apply to our case because the patient's hormonal condition (PAC and PRA) and blood pressure level have remained unchanged during the observation period. Factors (d) and (e) are unlikely to be the mechanisms underlying the normotension in our patient based on her medical history and physical findings (salt intake: approximately 11 g/day and BMI: approximately 24.9). Factor (c) indicates that excessive aldosterone secretion induces relative hypertension, but the blood pressure may remain in the normal range because of very low spontaneous baseline blood pressure levels. It is likely that factor (c) may apply to our case.

【Conclusion】

One important remaining question is why excessive hormone secretion did not affect the cardiovascular status of this patient. In this regard, several possible mechanisms have been reported including mineralocorticoid resistance. Further study is going to resolve this issue.