CEN Case Reports (2018) 7:77–82
https://doi.org/10.1007/s13730-017-0299-5

CASE REPORT

# Complete remission of hypertension in a hemodialysis patient after adrenalectomy for primary aldosteronism and renal transplantation

**Daisuke Watanabe[1] · Satoshi Morimoto[1] · Noriyoshi Takano[1] · Shihori Kimura[1] · Yasufumi Seki[1] · Kanako Bokuda[1] · Midori Sasaki-Yatabe[1] · Junichi Yatabe[1] · Hiromi Onizuka[2] · Tomoko Yamamoto[2] · Takashi Ando[1] · Atsuhiro Ichihara[1]**

Received: 20 September 2017 / Accepted: 25 December 2017 / Published online: 29 December 2017


**Abstract**
A 64-year-old man was admitted to our hospital for the hormonal evaluation of a right adrenal adenoma. He had been diagnosed with severe proteinuria and hypertension, and antihypertensive treatment was started at the age of 60. His renal function gradually declined, and hemodialysis was begun at the age of 64. Since his blood pressure was uncontrollable and resistant to antihypertensive treatment, an endocrinological examination was performed for an incidental right adrenal mass detected by computed tomography. The results of screening, including captopril challenge and an adrenocorticotropin stimulation test for primary aldosteronism, and adrenal venous sampling suggested excessive aldosterone secretion from the right adrenal gland. Adrenalectomy was performed; his blood pressure decreased and became well-controlled with a reduced antihypertensive regimen. Furthermore, he received renal transplantation which resulted in normalization of his serum potassium level, improvement of renal function and hormonal levels such as plasma renin activity and aldosterone concentration, and satisfactory blood pressure without any antihypertensive medications. This case is extremely important to demonstrate the effects of adrenalectomy for primary aldosteronism in a hemodialysis patient. It is possible that adrenalectomy may be a useful treatment for primary aldosteronism even in patients undergoing hemodialysis. Careful long-term follow-up of our case and investigations of the efficacy of adrenalectomy in similar cases are needed to address this issue.

**Keywords** Aldosterone · Blood pressure · Surgery · Renin · End-stage renal disease

## Introduction

In patients with primary aldosteronism (PA) undergoing hemodialysis, it is hard to expect normalization of high blood pressure even after adrenalectomy due to the existence of renal parenchymal hypertension. These patients are at high risk for cardiovascular complications in addition to hypertension. Therefore, ongoing debate exists on whether adrenalectomy is recommended for the treatment of patients with PA undergoing hemodialysis. Herein, we report a very rare and valuable case of PA due to unilateral adrenal adenoma, in which complete remission of hypertension occurred after adrenalectomy and renal transplantation.

✉ Satoshi Morimoto
smorimoto@endm.twmu.ac.jp

[1] Department of Endocrinology and Hypertension, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan

[2] Department of Pathology, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan

## Clinical course

A 64-year-old man was admitted to our hospital for hormonal evaluation of a right adrenal adenoma that was detected by abdominal computed tomography (CT). He had been having hypertension for 15 years and revealed proteinuria (0.5 g/gCre) without microscopic hematuria or casts with renal impairment (serum creatinine 5.36 mg/dL) which was too severe to be applicable for renal biopsy at the age of 60. He was diagnosed to have hypertensive nephrosclerosis clinically after ruling out other diseases to cause secondary kidney diseases including collagen diseases, hepatitis B or C, amyloidosis, and diabetes mellitus and antihypertensive treatment was started. However, his renal function gradually

declined, until, finally, hemodialysis was begun at the age of 64.

On admission, physical examination showed that his height was 180.5 cm and body weight was 84.5 kg. His blood pressure was 152/98 mmHg and pulse rate was 72 beats per minute under treatment with oral antihypertensive drugs such as amlodipine, a calcium channel blocker (CCB), and telmisartan, an angiotensin II receptor blocker (ARB). Laboratory and endocrinological findings are shown in Tables 1, 2 and 3. Laboratory findings revealed: hemoglobin 11.4 g/dL, serum sodium 141 mEq/L, potassium 4.2 mEq/L, calcium 7.5 mg/dL, inorganic phosphorus 5.8 mg/dL, creatinine 7.05 mg/dL, and hemoglobin A1c 5.1%. Calcium–phosphorus imbalance appeared due to chronic kidney disease, while his serum potassium level remained within normal range in spite of his renal dysfunction. Chest X-ray and echocardiography revealed mild cardiomegaly and moderately reduced left ventricular contraction, respectively. Plain CT imaging revealed a low-density mass of 20 mm in diameter on the right adrenal gland (Fig. 1). Endocrinological findings were as follows (Table 2): intact parathyroid hormone was elevated (492 pg/mL) due to secondary hyperparathyroidism.

**Table 1** Laboratory findings on admission

| | | | |
|---|---|---|---|
| Urinalysis: occult blood (1+), protein (3+), sugar (1+), RBC 1–4/HPF, cast (−) | | | |
| Urine volume: 1200 mL/day, urinary protein: 0.8 g/day | | | |
| Complete blood cell count | | | |
| WBC | 5840/μL | Hb | 11.4 g/dL |
| RBC | $3.00\times10^6$/μL | Plt | $14.2\times10^4$/μL |
| Blood chemistry | | | |
| TP | 5.9 g/dL | Cr | 7.05 mg/dL |
| Alb | 3.4 g/dL | PG | 135 mg/dL |
| AST | 14 IU/L | Na | 141 mEq/L |
| ALT | 23 IU/L | K | 4.2 mEq/L |
| LDH | 305 IU/L | Cl | 113 mEq/L |
| ALP | 235 IU/L | Ca | 7.5 mg/dL |
| γ-GTP | 26 IU/L | P | 5.8 mg/dL |
| CPK | 163 U/L | Mg | 2.0 mg/dL |
| Amy | 117 U/L | CRP | < 0.04 mg/dL |
| HDL-cho | 44 mg/dL | IgG | 996 mg/dL |
| LDL-cho | 66 mg/dL | IgA | 239 mg/dL |
| TG | 90 mg/dL | IgM | 62 mg/dL |
| BUN | 72.8 mg/dL | HbA1c | 5.1% |

*RBC* red blood cell, *HPF* high power field, *WBC* white blood cell, *Hb* hemoglobin, *Plt* platelet, *TP* total protein, *Alb* albumin, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *LDH* lactate dehydrogenase, *ALP* alkaline phosphatase, *γ-GTP* gamma-glutamyl transpeptidase, *CPK* creatine phosphokinase, *Amy*. amylase, *HDL-cho* high-density lipoprotein-cholesterol, *LDL-cho* low-density lipoprotein-cholesterol, *TG* triglyceride, *BUN* blood urea nitrogen, *Cre* creatinine, *PG* plasma glucose, *CRP* C reactive protein, *Ig* immunoglobulin, *HbA1c* hemoglobin A1c

**Table 2** Endocrinological examinations on admission

| | | Normal value |
|---|---|---|
| Intact-PTH | 492 pg/mL | 16–65 |
| fT3 | 2.43 pg/mL | 2.30–4.30 |
| fT4 | 1.08 ng/dL | 0.94–1.60 |
| TSH | 2.68 mU/mL | 0.38–4.30 |
| ACTH | 42.1 pg/mL | 7.4–55.7 |
| Cortisol | 20.5 μg/dL | 4.0–18.3 |
| PRA | < 0.1 ng/mL/h | 0.3–2.9 |
| PAC | 320 pg/mL | 29.9–159 |
| Epinephrine | 12 pg/mL | < 100 |
| Norepinephrine | 74 pg/mL | 100–450 |
| Dopamine | 20 pg/mL | < 20 |
| Urinary epinephrine | 2.6 μg/day | 3.0–15.0 |
| Urinary norepinephrine | 74 μg/day | 26–121 |
| Urinary dopamine | 381.2 μg/day | 190–740 |

*PTH* parathyroid, *fT3* free triiodothyronine, *fT4* free thyroxine, *TSH* thyroid stimulating hormone, *ACTH* adrenocorticotrophic hormone, *PRA* plasma renin activity, *PAC* plasma aldosterone concentration

His cortisol was slightly elevated (20.5 μg/dL), however, adrenocorticotrophic hormone (ACTH) was not suppressed (42.1 pg/mL). Adrenomedullary functions (plasma epinephrine, 12 pg/mL; plasma norepinephrine 74 pg/mL; urinary epinephrine excretion, 2.6 μg/day; urinary norepinephrine excretion, 74 μg/day) were normal. Plasma renin activity (PRA) was suppressed, accompanied by elevation of plasma aldosterone concentration (PAC) (PRA, < 0.1 ng/mL/h; PAC, 320 pg/mL), resulting in elevation of the PAC to PRA ratio to over 200, suggesting that the right adrenal mass was an aldosterone-producing adenoma. Therefore, an endocrinological screening test for PA was performed after admission to our hospital without discontinuing the CCB and ARB. The results of the captopril challenge test (PAC to PRA ratio was over 200 at 60 and 90 min after stimulation) and ACTH stimulation test (max PAC to cortisol ratio was 11.5) met the clinical criteria for the diagnosis of PA (Table 3). Therefore, adrenal venous sampling (AVS) was performed. The results of AVS, after ACTH loading, were as follows: PAC and cortisol values were 66100 pg/mL and 1519 μg/dL in the right adrenal vein and 977 pg/mL and 82.4 μg/dL in the left adrenal vein, respectively. The lateralized ratio (PAC to cortisol ratio of the right adrenal vein/PAC to cortisol ratio of the left adrenal vein) was 3.66, and the contralateral ratio (PAC to cortisol ratio of the left adrenal vein/PAC to cortisol ratio of the inferior vena cava) was 2.43. Although the contralateral ratio was not indicative of excessive secretion of aldosterone from the right adrenal mass, the apparently high absolute PAC value at the right adrenal vein suggested excessive aldosterone secretion from the right adrenal gland. The patient was not treated with mineralocorticoid receptor

**Table 3** Endocrinological test results

| | 0 | 60 min | 90 min |
|---|---|---|---|
| (A) Captopril challenge test | | | |
| PAC (pg/mL) | 190 | 125 | 143 |
| PRA (ng/mL/h) | 0.3 | 0.4 | 0.3 |
| ARR | 633.3 | 312.5 | 476.7 |
| | 0 | 30 min | 60 min |
| (B) ACTH stimulation test | | | |
| PAC (pg/mL) | 178 | 353 | 325 |
| Cortisol (μg/dL) | 17.6 | 30.6 | 32.52 |
| PAC/Cortisol | 10.1 | 11.5 | 10 |

*PRA* plasma renin activity, *PAC* plasma aldosterone concentration, *ARR* aldosterone to renin ratio, *ACTH* adrenocorticotrophic hormone

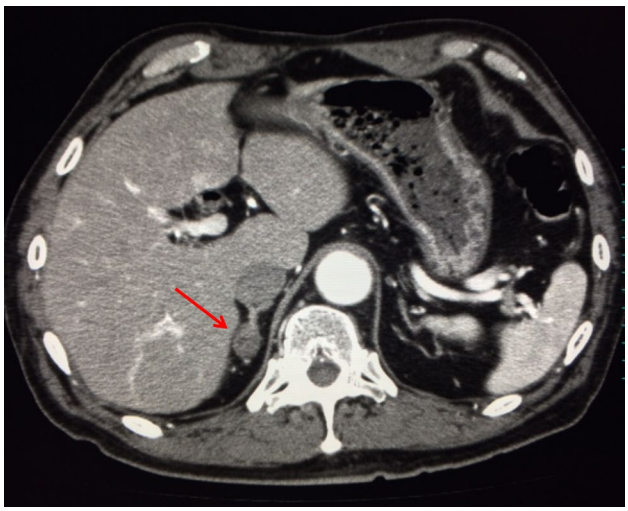

**Fig. 1** Abdominal computed tomography. Arrow indicates a low-density tumor on the right adrenal gland

antagonists (MRAs) before adrenalectomy, because it was performed just after the diagnosis was made. Right adrenalectomy was performed; pathologically, macroscopic feature of the cut surface showed a bright yellowish solid mass. Additionally, the adrenal mass was composed mainly of clear cells with positive immunoreactivity for adrenal aldosterone synthase enzyme (CYP11B2), consistent with pathological diagnosis of an aldosterone-producing adenoma (Fig. 2a–c). After right adrenalectomy, the patient's blood pressure declined gradually without administration of ARB or methyldopa, and the dosage of CCB was reduced (Fig. 3). After receiving renal transplantation, blood testing revealed that the patient's creatinine level had decreased to 1.06 mg/dL, and his blood pressure returned to the normal range without any antihypertensive medications. Additionally, in terms of hormonal changes, PAC decreased from 320 to 211 pg/mL and PRA rose from < 0.1 to 2.8 ng/mL/h.

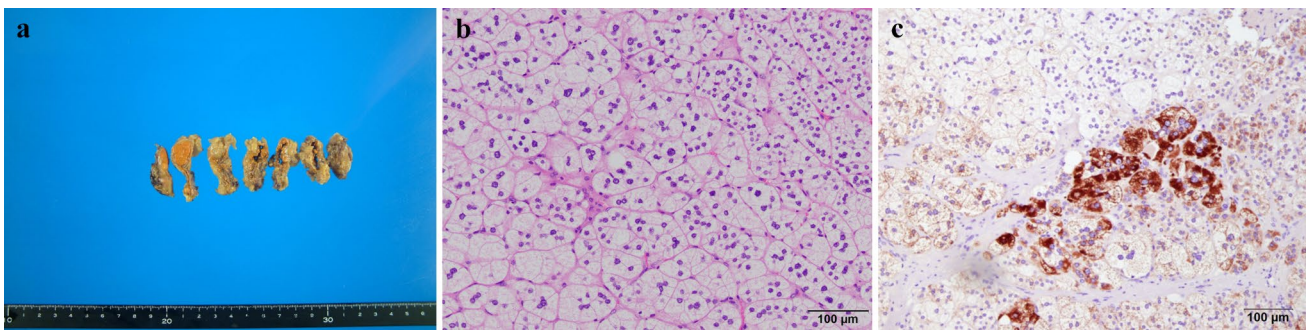


**Fig. 2** Pathological examination of the resected right adrenal specimen. **a** Macroscopic feature of the cut surface showed a bright yellowish solid mass, measuring 1.4 cm × 1.0 cm across. **b** Adrenal mass was composed mainly of clear cells (hematoxylin and eosin stain, scale bar is 100 μm). **c** Immunohistochemical staining showed compact cells were positive for CYP11B2 (dilution of 1:20, scale bar is 100 μm)

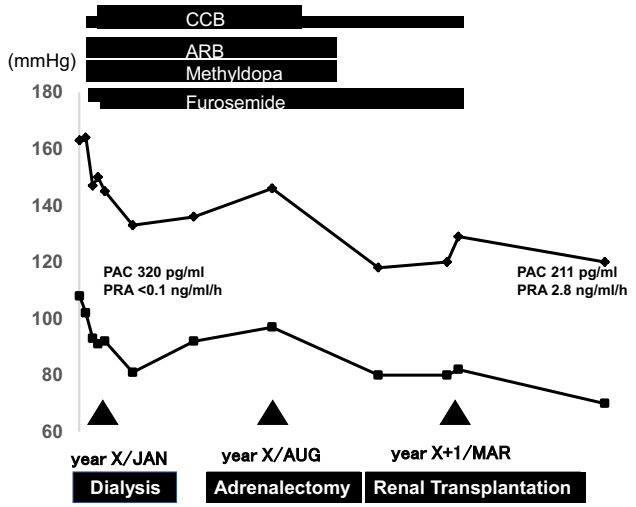


**Fig. 3** Clinical course of the current case. Filled diamond, systolic blood pressure; filled square, diastolic blood pressure. *CCB* calcium channel blocker, *ARB* angiotensin II receptor blocker, *PAC* plasma aldosterone concentration, *PRA* plasma renin activity, *sBP* systolic blood pressure, *dBP* diastolic blood pressure

## Discussion

Although several tests are recommended for the diagnosis of PA, the testing conditions such as medications, potassium status, and dietary sodium, etc., interfere with the results of these tests [1]. In hemodialysis patients having impaired renal function and an altered renin-angiotensin-aldosterone system (RAS) and potassium balance, the diagnosis of PA is difficult.

In dialysis patients, the elevation of aldosterone level which was triggered by the electrolyte imbalance may be observed. Consequently, this hormonal environment may affect the interpretation of AVS data. The contralateral ratio calculated by AVS data display the degree of suppressed aldosterone level in the unaffected adrenal gland. Taking the elevated circulating aldosterone level in ESRD patients into consideration, we presume that the degree of suppressed aldosterone level could be masked in the unaffected adrenal gland. Therefore, in end-stage renal disease (ESRD) patients, contralateral ratio is unreliable for the interpretation of AVS data.

It has been reported that PA patients have a higher prevalence rate of cardiovascular damage than age- and blood pressure-matched patients with essential hypertension [2]. In addition, PA patients have greater renal damage than patients with essential hypertension [3]. The glomerular filtration rate (GFR) has been shown to be increased in PA patients [4]. Normalization of aldosterone excess by either adrenalectomy or MRAs restores intrarenal hemodynamics, corrects GFR, and decreases urinary albumin excretion [4]. Although GFR decreases during the initial few months after either surgical or medical treatment, renoprotective outcomes can be expected in the long term in these patients [5]. Therefore, it is possible that these treatments may be significant in protecting renal function in predialysis chronic kidney disease patients and renal transplant patients.

Long-term elevations of aldosterone occur in hemodialysis patients [6]. Aldosterone induces early atherosclerosis and promotes inflammation through the activation of mineralocorticoid receptor-regulated genes [7]. A significant correlation between PAC and left ventricular mass has been observed in hemodialysis patients [8]. Therefore, an excess of aldosterone in hemodialysis may be a therapeutic target for MRAs. Previous reports have demonstrated that administration of MRAs decreased predialysis systolic blood pressure in hemodialysis patients, especially in oligo-anuric patients, without changes in predialysis or postdialysis serum potassium, PAC or PRA [9, 10]. These findings suggest that MRAs lower blood pressure by the antagonism of non- and extra-renal mineralocorticoid receptors or interactions with glucocorticoid receptors [11]. Although MRAs increase the possibility of risk for hyperkalemia, a previous clinical study demonstrated that low-dose MRAs lower blood pressure and concomitantly improve left ventricular ejection fraction and hypertrophy in maintenance hemodialysis patients [6]. Low-dose MRAs have been found to reduce cardio-cerebrovascular events and all-cause mortality in hemodialysis patients [12]. Although the potential benefits of the use of MRAs in hemodialysis patients need further study, the blockade of mineralocorticoid receptors may be profitable in managing these patients.

The disparity of the long-term effects on cardiovascular events between adrenalectomy and MR antagonist treatment remains undetermined. However, it has been reported that surgical treatment is significantly associated with amelioration of hypokalemia and secondary hypertension in patients with unilateral PA [13]. Additionally, risk of hyperkalemia may be higher among MRA-treated patients undergoing hemodialysis. Therefore, it could be possible that unilateral adrenalectomy may be more beneficial for PA patients undergoing hemodialysis than MR antagonist treatment. However, hemodialysis contributes to the risk of postoperative mortality and was considered as high risk group for anesthesia [14]. If the risk of postoperative severe morbidity and mortality is predicted before operation, the MR antagonist medication should be prior to surgical treatment. The patient did not have any special risk for anesthesia or operation. For these reasons, we selected adrenalectomy for this patient.

Recent studies have indicated a high prevalence of PA in hypertensive patients [15]. It is possible that there is a high incidence of PA even in maintenance hemodialysis patients, although the incidence has not been well-documented. A couple of case reports have described PA diagnosed in

hemodialysis patients, to whom spironolactone treatments were administered but adrenalectomy was not performed [16, 17]. In addition, there are a couple of case reports describing PA patients on dialysis who underwent adrenalectomy. Kojima et al. [18] performed adrenalectomy in a hemodialysis patient with PA. They reported improvement of aldosterone excess, but did not comment on the blood pressure-lowering effect, because hypertension was not noted in this case. Nakada et al. [19] reported a peritoneal dialysis patient with PA who showed only slight decrease of blood pressure without achieving complete remission of hypertension after adrenalectomy. Therefore, there have been no case reports showing complete regression of hypertension after adrenalectomy for PA in dialysis patients. One of the reasons may be the fact that blood pressure normalization is difficult to achieve due to the existence of renal parenchymal hypertension. In the current case, the patient's blood pressure, in addition to serum potassium and hormonal levels, became normalized after adrenalectomy, which was performed in anticipation of cardiovascular and renoprotective effects and a post renal transplant blood pressure-lowering effect. Therefore, the current case is extremely important to demonstrate the effects of adrenalectomy for PA in a hemodialysis patient. This case showed the possibility that adrenalectomy for PA may be a useful treatment even in patients undergoing hemodialysis. Careful long-term follow-up of the current case and investigations of the efficacy of adrenalectomy in similar cases are needed to address this issue.

In conclusion, hemodialysis patients have a high prevalence of cardiovascular diseases. Overproduction of aldosterone may be associated with increased cardiovascular diseases in patients with ESRD. Therefore, when an adrenal mass is detected by abdominal imaging, a diagnosis of PA should be made carefully. In patients undergoing hemodialysis, the potassium balance, RAS and blood pressure levels are altered, making the diagnosis of PA difficult. If PA is diagnosed in hemodialysis patients, adrenalectomy in addition to renal transplantation may be an alternative strategy for the treatment of these patients. Future clinical studies investigating patients like ours need to be conducted to establish therapeutic criteria for PA in hemodialysis patients.

**Acknowledgements** We thank Dr Koshiro Nishimoto (Department of Uro-Oncology, Saitama Medical University International Medical Center) for the generous gift of CYP11B2 antibody and Noriko Morishima for her excellent technical support in immunohistochemical staining.

## Compliance with ethical standards

**Conflict of interest** All the authors have declared no competing interest.

**Human and animal rights** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** Informed consent was obtained from all the individual participants included in the study.

## References

1. Funder JW, Carey RM, Mantero F, Murad MH, Reincke M, Shibata H, Stowasser M, Young WF Jr. The management of primary aldosteronism: case detection, diagnosis, and treatment: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2016;101:1889–916.
2. Prejbisz A, Warchol-Celinska E, Lenders JW, Januszewicz A. Cardiovascular risk in primary hyperaldosteronism. Horm Metab Res. 2015;47:973–80.
3. Nishimura M, Uzu T, Fujii T, Kuroda S, Nakamura S, Inenaga T, Kimura G. Cardiovascular complications in patients with primary aldosteronism. Am J Kidney Dis. 1999;33:261–6.
4. Sechi LA, Di Fabio A, Bazzocchi M, Uzzau A, Catena C. Intrarenal hemodynamics in primary aldosteronism before and after treatment. J Clin Endocrinol Metab. 2009;94:1191–7.
5. Sechi LA, Novello M, Lapenna R, Baroselli S, Nadalini E, Colussi GL, Catena C. Long-term renal outcomes in patients with primary aldosteronism. JAMA. 2006;295:2638–45.
6. Quach K, Lvtvyn L, Baigent C, Bueti J, Garg AX, Hawley C, Haynes R, Manns B, Perkovic V, Rabbat CG, Wald R, Walsh M. The safety and efficacy of mineralocorticoid receptor antagonists in patients who require dialysis: a systematic review and meta-analysis. Am J Kidney Dis. 2016;68:591–8.
7. Briet M, Schiffrin EL. Vascular actions of aldosterone. J Vasc Res. 2013;50:89–99.
8. Sato A, Funder JW, Saruta T. Involvement of aldosterone in left ventricular hypertrophy of patients with end-stage renal failure treated with hemodialysis. Am J Hypertens. 1999;12:867–73.
9. Gross E, Rothstein M, Dombek S, Juknis HI. Effect of spironolactone on blood pressure and the renin–angiotensin–aldosterone system in oligo-anuric hemodialysis patients. Am J Kidney Dis. 2005;46:94–101.
10. Shavit L, Neykin D, Lifschitz M, Slotki I. Effect of eplerenone on blood pressure and the renin–angiotensin–aldosterone system in oligo-anuric chronic hemodialysis patients—a pilot study. Clin Nephrol. 2011;76:388 – 95.
11. Suthar SD, Middleton JP. Clinical outcomes in dialysis patients: prospects for improvement with aldosterone receptor antagonists. Semin Dial. 2016;29:52–61.
12. Matsumoto Y, Mori Y, Kageyama S, Arihara K, Sugiyama T, Ohmura H, Yakushigawa T, Sugiyama H, Shimada Y, Nojima Y, Shio N. Spironolactone reduces cardiovascular and cerebrovascular morbidity and mortality in hemodialysis patients. J Am Coll Cardiol. 2014;63:528–36.
13. Miyake Y, Tanaka K, Nishikawa T, Naruse M, Takayanagi R, Sasano H, Takeda Y, Shibata H, Sone M, Satoh F, Yamada M, Ueshiba H, Katabami T, Iwasaki Y, Tanaka H, Tanahashi Y, Suzuki S, Hasegawa T, Katsumata N, Tajima T, Yanase T. Prognosis of primary aldosteronism in Japan: results from a nationwide epidemiological study. Endocr J. 2014;61:35–40.
14. Abe H. Mafune K. Risk factors for maintenance hemodialysis patients undergoing elective and emergency abdominal surgery. Surg Today. 2014;44:1906–11.
15. Omura M, Saito J, Yamaguchi K, Kakuta Y, Nishikawa T. Prospective study on the prevalence of secondary hypertension among hypertensive patients visiting a general outpatient clinic in Japan. Hypertens Res. 2004;27:193–202.
16. Matsuda K, Shimamoto K, Ura N, Ogata H, Shizukuda Y, Iwakura M, Nozawa A, Kikuchi K, Iimura O. A case of primary

aldosteronism with chronic renal failure undergoing hemodialysis treatment. Endocrinol Jpn. 1989;36:681–6.
17. Kazory A, Weiner ID. Primary hyperaldosteronism in a patient with end-stage renal disease. Nephrol Dial Transplant. 2007;22:917–9.
18. Kojima Y, Miyake O, Morimoto A, Kawamura C, Katayama S. A case of aldosterone-producing adenoma associated with end-stage renal disease. Hinyokika Kiyo. 2010;56:21–4.
19. Nakada T, Kimura M. Primary aldosteronism associated with chronic renal failure. Report of a case. Int Urol Nephrol. 1984;16:165–73.