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Fortuitous Hormonal Ablation of Adrenal Aldosteronoma due to a Complication, Adrenal Venous Infarction by Adrenal Venography during Adrenal Vein Sampling: Case Report

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Abstract

A 61-year-old woman was admitted to our Department for examination of uncontrollable hypertension. An aldosterone-producing adenoma (aldosteronomas) was suspected based on her hypertension, low plasma renin activity and a right adrenal mass on CT, although plasma and urinary aldosterone levels were within normal ranges. Because of the ambiguous hormonal results, we performed adrenal vein sampling including bilateral adrenal veins and the inferior vena cava. The results of aldosterone and cortisol levels of the blood samples reported later confirmed an aldosteronomas in the right adrenal gland. Immediately after the second right adrenal venography after successful sampling followed by the first uneventful right venography, the patient complained of back pain and CT revealed the swollen right adrenal gland with high density, suggesting a complication of intra-adrenal hemorrhagic venous infarction. Thereafter, her hypertension improved, plasma aldosterone levels decreased to a lower normal limit, and plasma renin activity returned to a normal range. CT obtained 3 months later and adrenocortical scintigraphy performed 6 months later revealed that most of the aldosteronoma was necrotic. During the 9-months follow-up period, hormonal ablation of the aldosteronoma was maintained. Although hormonal ablation of the aldosteronoma was fortuitously obtained in our case, adrenal venography should be performed with meticulous care and after confirmation of smooth blood flow into the syringe connected with the catheter by pulling the plunger. Manual injection of the contrast medium into the adrenal vein should be made as gentle and slow as possible to avoid complications, especially in case of prolonged wedge of the catheter tip in the adrenal vein.

Key words: adrenal gland, adrenal vein sampling, aldosteronoma, complication, primary aldosteronism, venography

Introduction

Primary aldosteronism, one of the causes of secondary hypertension, occurs in up to 3–15% of hypertensive patients[1]. The major subtypes of primary aldosteronism are aldosterone-producing adenoma (aldosteronoma), the frequency of which is nearly 60%, and that of idiopathic hyperaldosteronism (IHA) is 30% and the proportion with IHA has increased[2]. Treatment differs between these two major subtypes, as the former is typically removed in a surgical procedure, while the latter is treated with medication. Therefore, it is important to distinguish between aldosteronoma and IHA[3]. In general, after establishing primary aldosteronism by biochemical and hormonal findings, non-invasive imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and radionuclide imaging (RI) have been used for differential diagnosis. When results of those are indeterminate, adrenal vein sampling (AVS) is the most accurate method of indicating hormonal localization and

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function. However, complications such as intra- or extra-adrenal venous thrombosis and adrenal infarction are not rare[4]. In this report, we describe a case of aldosteronoma, in which adrenal venous infarction occurred by adrenal venography after successful vein sampling and caused fortuitously hormonal ablation of the aldosteronoma.

Case Report

A 61-year-old woman with hypertension was referred to our Department. Her past history included poorly controlled hypertension for 30 years and cerebral infarction at the age of 50. The patient had been treated with antihypertensive medications, including an angiotensin-converting enzyme (ACE) inhibitor, a beta-blocker, a calcium-channel blocker, and an aldosterone antagonist. Primary aldosteronism was suspected based on her hypertension and suppressed plasma renin activity (0.1 - 0.2 ng/ml/h, normal range, 0.3–2.9 ng/ml/h). However, the concentrations of plasma aldosterone (215 pg/ml, normal range 35.7–240 pg/ml), and urinary aldosterone (9.9 μg/day, normal range $\leq$10 μg/day) were in the upper normal limits, and serum potassium level was also within a normal range. Her blood pressure was high in a range of 170–220/70–110 mmHg.

CT scanning demonstrated a right adrenal lipid-rich mass that was 15 mm $\times$ 11 mm in size on unenhanced CT images (Fig. 1A). The mass demonstrated marked

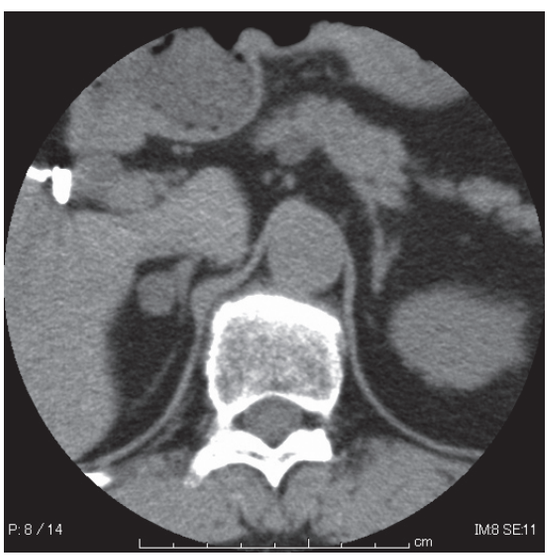

Fig. 1A

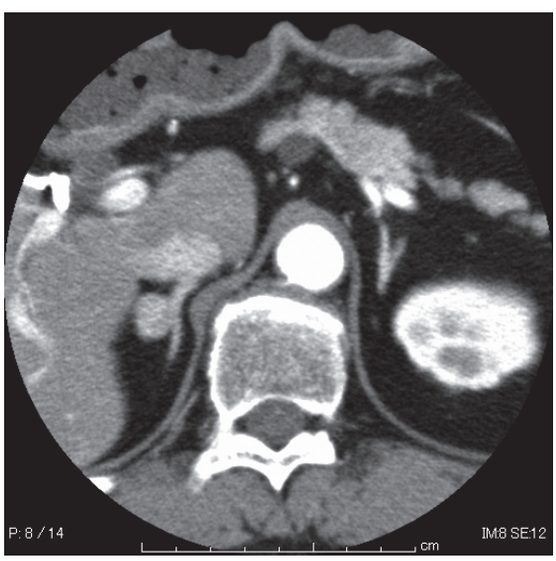

Fig. 1B

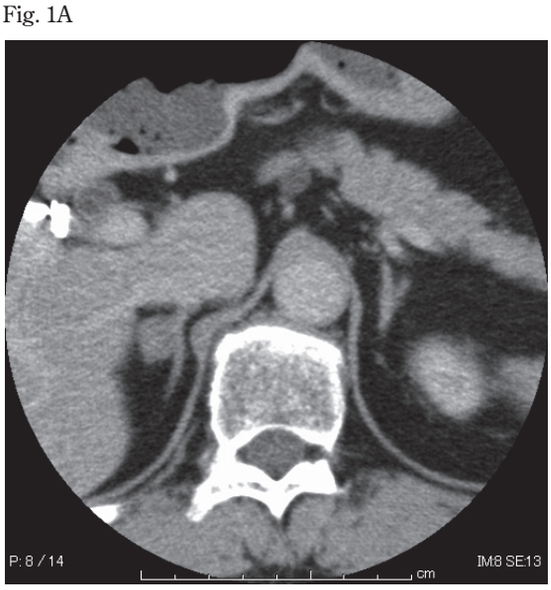

Fig. 1C

Fig. 1. Dynamic CT scanning. A : Unenhanced CT image shows a low density (9HU) mass (arrow), 15mm×11mm in size, in the right adrenal gland. B: Contrast-enhanced30-second CT image shows marked enhancement (127HU) of the mass (arrow). C: Contrast-enhanced 300-second CT image shows rapid washout of contrast medium from the mass (47HU) (arrow).

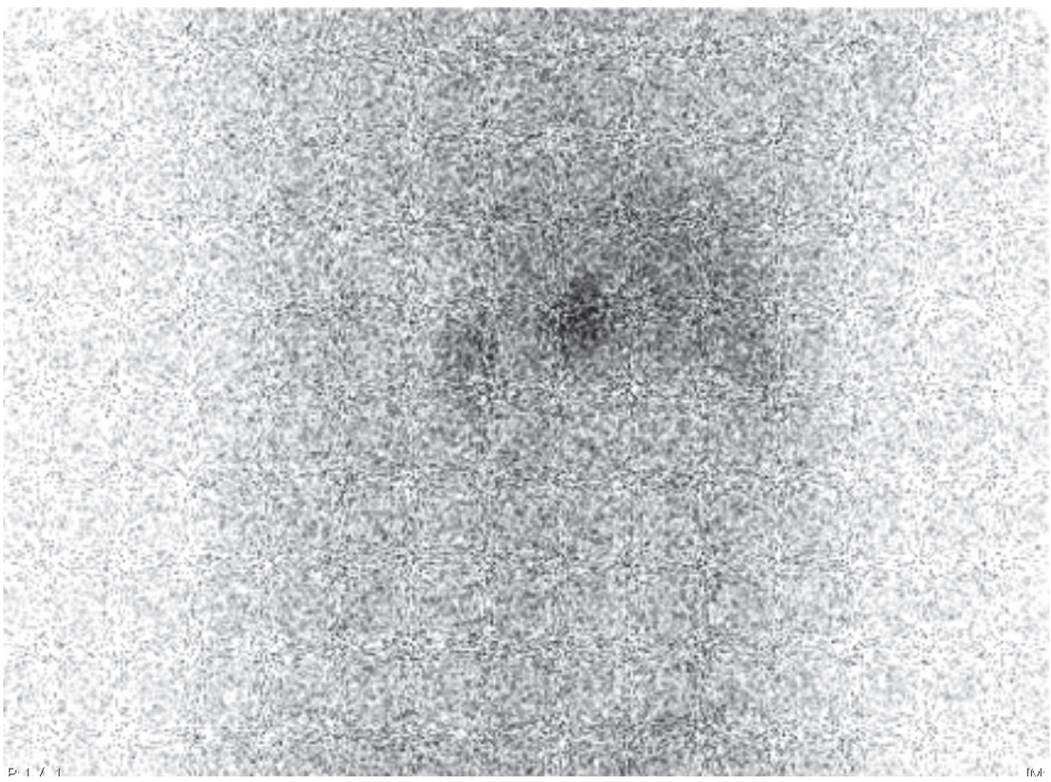

Fig. 2. ^{131}I-adosterol adrenocortical scintigraphy performed before the adrenal vein sampling. Posterior view of the abdomen shows intense ^{131}I-adosterol uptake in the right adrenal gland containing an adenoma (arrow).

enhancement 30 seconds after starting injection of contrast medium (Fig. 1B) and rapid washout of the medium at 300 seconds (Fig. 1C). An ^{131}I-adosterol adrenocortical scan demonstrated intense uptake in the right mass-bearing adrenal gland (Fig. 2). These CT and RI examinations suggested that the right adrenal mass was an adenoma. Because of the equivocal results in hormonal examinations, AVS was performed to differentiate an aldosteronoma from a silent adenoma after obtaining written informed consent from her. The sampling was first performed for the left adrenal vein and the inferior vena cava. Seven ml of blood was sampled each through the 5 Fr. modified cobra shaped catheter (Hanako Med. Co., Saitama, Japan) from the left adrenal vein and the inferior vena cava. It took about 5 minutes each. Then the right adrenal vein was catheterized with the 5 Fr. shepherd hook catheter (Hanako Med. Co., Saitama, Japan) and its venous blood was sampled successfully after confirmation of the catheter tip in the right adrenal vein by the first adrenal venography with manual injection of 3 ml of contrast medium. After venography, 2 ml of heparinized physiological saline was infused into the catheter to prevent blood coagulation. Then the 7 ml of blood from the right adrenal vein dripped for sampling. It took about 15 minutes. The hormonal (aldosterone and cortisol) results of AVS including bilateral adrenal veins and the inferior vena cava reported later confirmed an aldosteronoma in the right adrenal gland (Table 1). When manual injection of 1 cc of contrast medium was made again into the right

Table 1. Results of adrenal vein sampling.

Location	Aldosterone (ng/dl)	Cortisol (μ g/dl)	Aldosterone/cortisol ratio
Right adrenal vein	17,800	60.8	292.8
Left adrenal vein	165	21.9	7.5
Inferior vena cava	191	5.45	35.0

adrenal vein to reconfirm whether the catheter tip was placed in the right position after dripping the venous blood for sampling and pulling a small amount of blood through the catheter by a syringe, the patient complained of back pain. We performed CT examination 5 minutes after the back pain occurred, which showed swelling of the entire right adrenal gland with high density (Fig. 3).

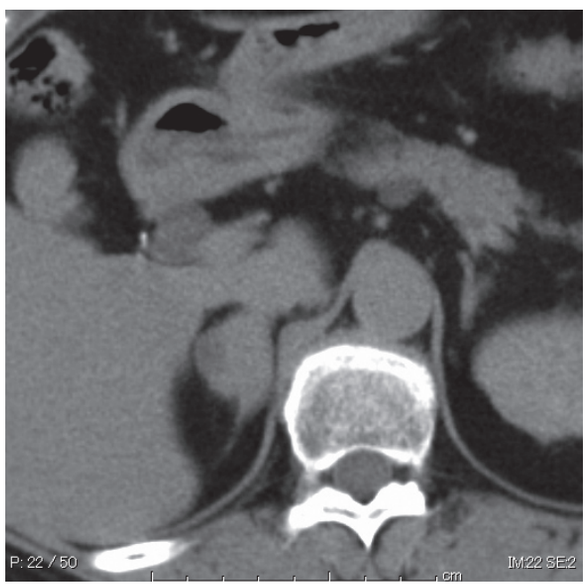

Fig. 3. Unhanced CT scanning immediately after the adrenal venography. The entire right adrenal gland (arrow) is swollen with high density (67 HU).

The pain was controlled by an anodyne. The patient was observed and followed carefully. Ten days after the AVS procedure, the plasma aldosterone level was remarkably decreased to the lower normal range and plasma renin activity rose to a normal level (Table 2). Further, her blood pressure was decreased to a range of 100-150/70-90mmHg by administration of reduced doses of a calcium-channel blocker and an angiotensin II type 1 (AT1) receptor blocker. Three months later, CT showed that the enhancement of the adenoma clearly decreased (Fig. 4), suggesting that most of the adenoma was necrotic. Improvement in hypertension, hormonal normalization and CT findings suggested that the adrenal venous infarction led to hormonal ablation of the aldosteronoma. Adrenal ablation was also demonstrated by adrenocortical imaging (Fig. 5). At the time of writing, hormonal ablation of the aldosteronoma has been continued for more than 9 months after the AVS.

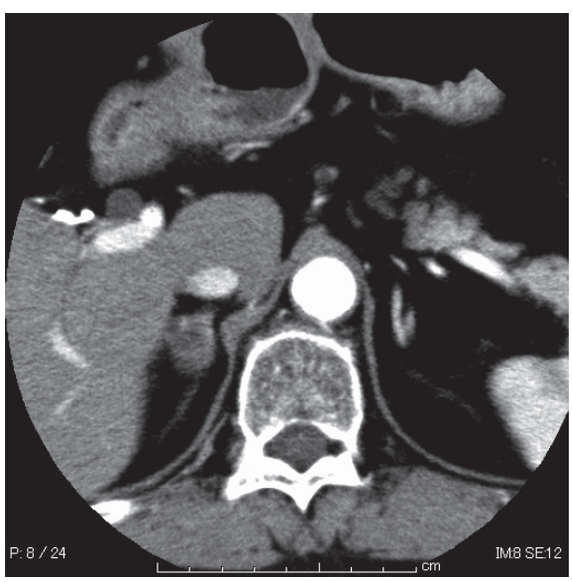

Fig. 4. Contrast-enhanced 30-second CT scan 3 months after the adrenal vein sampling. The right aldosteronoma-bearing adrenal gland has decreased to the untreated size and the adenoma enhances slightly (22HU), suggesting that most part of the adenoma has become necrotic (arrow).

Table 2. Blood hormonal and potassium data before and after adrenal vein sampling (AVS).

Examined item	Normal range	Examined value before and after AVS			
		Before	10 days	21 days	9 months
PAC*	35.7－240(pg/ml)	215	63.2	92.2	136
PRA†	0.3－2.9(ng/ml/h)	0.1	0.3	1.8	4.9
Serum K	3.6－4.9(mEq/l)	3.9	4.6	4.6	5.1

*Plasma aldosterone concentration. †Plasma renin activity.

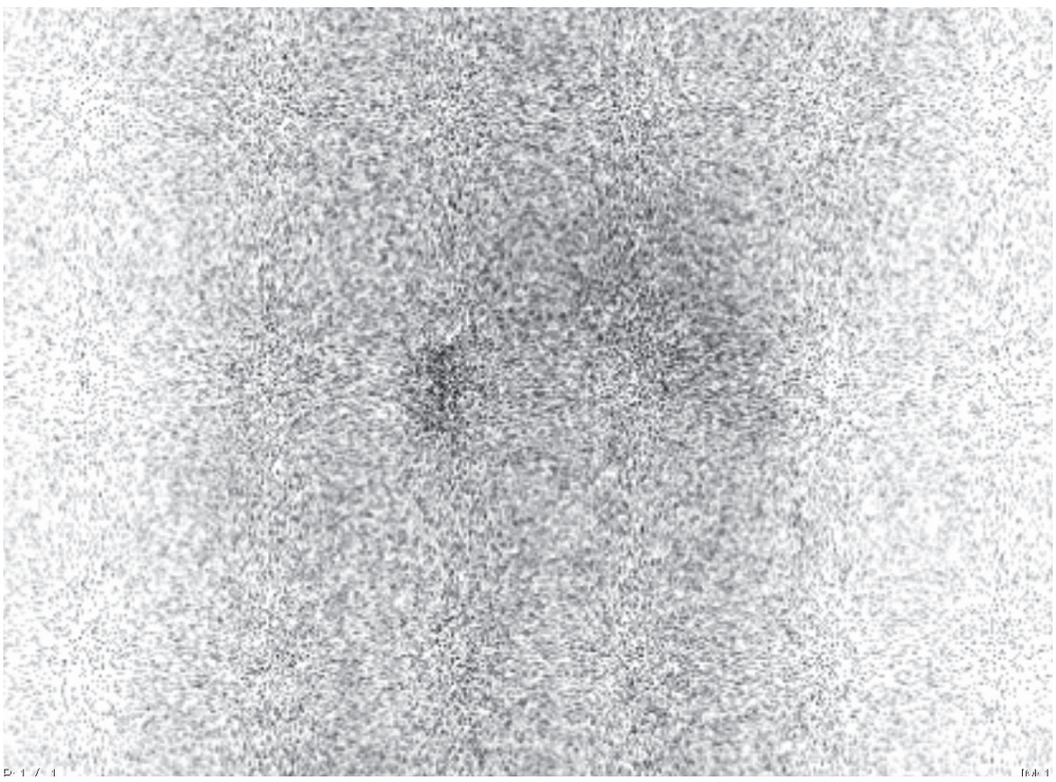

Fig. 5. ^{131}I-adosterol adrenocortical scintigraphy 6 months after the adrenal vein sampling. The right adrenal gland is no longer visible (arrow), suggesting that it is ablated.

Discussion

AVS is useful to differentiate between an aldosteronoma and IHA, as well as to localize an aldosteronoma. Treatment for these subtypes differs and it is essential to accurately diagnose the lesion. A recent study has shown that 21.7% of patients would have missed an appropriate adrenalectomy and 24.7% would have had an unnecessary adrenalectomy on the basis of CT findings alone[5]. In addition, CT scanning cannot reliably detect an adrenal adenoma with a diameter of less than 1 cm[6]. To avoid an unnecessary and inappropriate adrenalectomy, AVS is performed as a direct hormonal assessment for patients with negative or equivocal CT findings[6].

The accuracy of AVS has been reported to be greater than 90%[7]. However, it is an invasive procedure with more potential complications as compared with other procedures, such as CT scanning, MRI, and RI. In addition, catheterization of the adrenal veins requires a highly skilled technique, especially for the right adrenal vein. Complications such as intra- or extra- adrenal venous thrombosis and adrenal infarction have been reported to occur in some 5% of patients that undergo adrenal venography[4]. If both adrenal glands are infarcted completely, adrenal insufficiency may occur, whereas if the tumor- bearing gland is infarcted, hormonal ablation may occur[8].

Surgical removal is commonly recommended as treatment for an aldosteronoma. Transcatheter arterial embolization and CT-guided radiofrequency ablation are non-surgical alternative for therapy of aldosteronomas[9, 10]. Although there have been several reports of fortuitous remission of primary aldosteronism and Cushing's syndrome following adrenal venography [11–14], the attempts using vigorous retrograde injection of contrast material into the adrenal vein failed to infarct the aldosteronoma-containing gland in 4 systemically heparinized patients [8]. Systemic heparinization is not generally performed for AVS [1, 4–6, 11]. Heparinized physiological saline is usually infused into the catheter to prevent blood coagulation. We also performed AVS in our patient without systemic heparinization.

The venous blood from the right adrenal gland enters the inferior vena cava at an acute angle either as a single or as multiple channels, whereas the left adrenal vein enters the left renal vein. Therefore catheterization is

more difficult into the right adrenal vein than into the left adrenal vein. In addition, the catheter tip is apt to be wedged tightly in the right adrenal vein because of a small caliber. In our case, the catheter was successfully wedged in the right adrenal vein. Although, after dripping of the venous blood for sampling, the blood in the catheter was confirmed to flow into the syringe connected with the catheter by pulling the plunger, this confirmation might be insufficient for assessment of smooth blood flow from the right adrenal vein. Venous congestion might occur by the prolonged (15 minutes) wedge of the catheter tip. Under this condition, the injected contrast material might cause hemorrhagic infarction in the right adrenal gland. This assumption is supported by the initial success in the right adrenal venography and the CT findings that the right adrenal gland was swollen and the density of the entire adrenal gland increased on CT performed 5 minutes after injection of the contrast medium. The over-distension of the capillaries and the veins in the cortico − medullary plexus by the injection of contrast medium might rupture their thin walls and lead to hemorrhagic infarction or extravasation of contrast medium into the adrenal tissue[4]. However, as shown in the previous report[8], vigorous retrograde injection of contrast medium alone could not always produce adrenal infarction,. Preformed adrenal vein tiny thrombi might also be responsible for adrenal infarction in our case. If quick measurement of aldosterone and cortisol in the blood samples were possible on site in future, reconfirmation of the catheter tip by venography could be omitted.

Although hormonal ablation of the aldosteronoma was fortuitously obtained in our case, adrenal venography should be performed with meticulous care and after confirmation of smooth blood flow into the syringe connected with the catheter by pulling the plunger. Manual injection of the contrast medium into the adrenal vein should be also made as gentle and slow as possible to avoid complications, especially in case of prolonged wedge of the catheter tip in the adrenal vein.

References

1. Ishibashi T, Satoh F, Yamada T, Sato A, Matsuhashi T, Takase K. Primary aldosteronism: a pictorial essay. Abdom Imaging 2007; 32: 504–14.
2. Fehaily MA, Duh QY. Clinical manifestation of aldosteronoma. Surg Clin N Am 2004; 84: 887–905.
3. Tan YY, Ogilvie JB, Triponez F, Caron NR, Kebebew EK, Clark OH, et al. Selective use of adrenal venous sampling in the lateralization of aldosterone-producing adenomas. World J Surg 2006; 30: 879–85.
4. Bayliss RIS, Edwards OM, Starer F. Complications of adrenal venography. Br J Radiol 1970; 43: 531–3.
5. Young WF, Stanson AW, Thompson GB, Grant CS, Farley DR, van Heerden JA. Role for adrenal venous sampling in primary aldosteronism. Surgery 2004; 136: 1227–35.
6. Toniato A, Bernante P, Rossi GP, Pelizzo MR. The role of adrenal venous sampling in the surgical management of primary aldosteronism. World J Surg 2006; 30: 624–7.
7. Doppman JL, Gill JR, Miller DL, Chang R, Gupta R, Friedman TC, et al. Distinction between hyperaldosteronism due to bilateral hyperplasia and unilateral aldosteronoma: reliability of CT. Radiology 1992; 184: 677–82.
8. Dunnick NR, Doppman JL, Gill JR Jr. Failure to ablate the adrenal gland by injection of contrast material. Radiology 1982; 142: 67–9.
9. Hokotate H, Inoue H, Baba Y, Tsuchimochi S, Nakajo M. Aldosteronomas: experience with superselective adrenal arterial embolization in 33 Cases. Radiology 2003; 227: 401–6.
10. Mayo-Smith WW, Dupuy DE. Adrenal neoplasms: CT-guided radiofrequency ablation—preliminary results. Radiology 2004; 231: 225–30.
11. Fisher CE, Turner FA, Horton R. Remission of primary hyperaldosteronism after adrenal venography. N Eng J Med 1971; 285: 334–6.
12. Fellerman H, Dalakos TG, Streeten DHP. Remission of Cushing's syndrome after unilateral adrenal phlebography. apparent destruction of adrenal adenoma. Ann Intern Med 1970; 73: 585–9.
13. Melby JC. Identifying the adrenal lesion in primary aldosteronism. Ann Intern Med 1972; 76: 1039–41.
14. Taylor HC, Sachs CR. Primary aldosteronism: Remission and development of adrenal insufficiency after adrenal venography. Ann Intern Med 1976; 85: 207–9.

副腎静脈血サンプリングにおける副腎静脈造影による合併症の副腎静脈梗塞で偶然に治療効果を認めた原発性アルドステロン症の１例

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症例は61歳の女性で，降圧剤にてコントロール不良の高血圧を主訴に精査目的で入院となった．血漿および尿中アルドステロン値は正常範囲であったが，高血圧，低レニン血症，ＣＴにて右副腎腫瘍を認め，原発性アルドステロン症の腺腫（アルドステロノーマ）が疑われた．ホルモンデータが原発性アルドステロン症の診断に確定的でなかったため，静脈血サンプリングが行われた．左右副腎静脈と下大静脈のサンプリング血のアルドステロンとコルチゾールの値より右副腎のアルドステロノーマの診断が得られた．サンプリングのための最初の静脈造影では何も生じなかったが，最後に行われた右副腎静脈血サンプリングが終了後，右副腎静脈のカテーテルの先端の位置を再確認する目的で施行した２回目の静脈造影直後，患者が背部痛を訴えた．その直後の単純ＣＴで右副腎の全体的腫大とＣＴ値の上昇を認め，造影剤の副腎内静脈外漏出による出血性静脈梗塞が疑われた．患者の痛みは保存的治療で軽快した．経過観察で血漿アルドステロンは正常上限値から下限値へと低下，レニン活性は正常化し，血圧コントロールも容易となった．３ヶ月後のＣＴでは右副腎のアルドステロノーマの造影効果はほとんど認められず，６ヶ月後の副腎皮質シンチグラフィでは右副腎はアルドステロノーマを含め，描出されなかった．以上より右副腎の出血性静脈梗塞によりアルドステロノーマの壊死が生じ，アルドステロン産生能が低下したと考えられた．過去に同様の治療効果が数例報告されている一方，副腎静脈から逆行性に造影剤を意図的に急速静注し，アルドステロノーマを梗塞壊死に陥らせる試みがなされているが，失敗している．この試みは全身のヘパリナイゼーション下で行われているが，通常副腎静脈サンプリングでは全身のヘパリナイゼーションは行われず，本例も行っていない．ヘパリナイゼーション下で静脈梗塞が生じなかったことを考えると，静脈血栓形成も梗塞に関与した可能性もある．副腎静脈サンプリングは原発性アルドステロン症の局在，鑑別診断に優れた検査法であるが，副腎静脈梗塞などの合併症も少なくない．このような合併症を防ぐために，副腎静脈サンプリング検査には細心の注意を払い，カテーテルと接続した注射器で血液が抵抗なく吸引できることを確認して行うべきである．特にカテーテル先端が副腎静脈に長く留まる場合は可能な限り穏やかにかつ緩徐に造影剤を注入するべきと考えられる．