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Case Report

A Rare Independent Left Inferior Phrenic Vein Sampling in a Left Adrenal Aldosterone-Producing Adenoma ☆

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ABSTRACT

This report presents a case of left adrenal aldosterone-producing adenoma (APA) diagnosed by segmental adrenal venous sampling in a patient with primary aldosteronism and a rare venous anomaly in which the left inferior phrenic vein (LIPV) and adrenal central vein entered the left renal vein separately. The outflow of tumor blood into the LIPV and the specimen from the LIPV that showed much higher aldosterone level than that from the adrenal central vein and tributaries were useful for proving the aldosterone hypersecretion from the APA. Sampling from the LIPV could be of diagnostic value for left APA.

Introduction

Primary aldosteronism (PA) is the most common cause of secondary hypertension, accounting for 3% to 10% of all hypertension cases [1,2]. Adrenal venous sampling (AVS) is the standard method of subtyping and diagnosing unilateral lesions that are curable by surgery and bilateral lesions that are treatable with medical therapy [3]. On the left side, blood sampling from the common trunk in conjunction with both the left adrenal central vein (LCV) and left inferior phrenic vein (LIPV) and the LCV is recommended in the Endocrine Society Clinical Guidelines [2] and Japan Endocrine Society Guidelines [1], respectively. However, the significance of sampling from the LIPV is not well known.

Anatomically, the LIPV does not form a common trunk with the left adrenal vein but enters the left renal vein independently [4-6]. This is thought to be rare, but the actual frequency is unknown [7,8]. In this report, we present a case in which the LIPV was not merged with the LCV in a patient with high levels of aldosterone due to a left aldosterone-producing adenoma (APA). In addition, we present an interesting finding regarding

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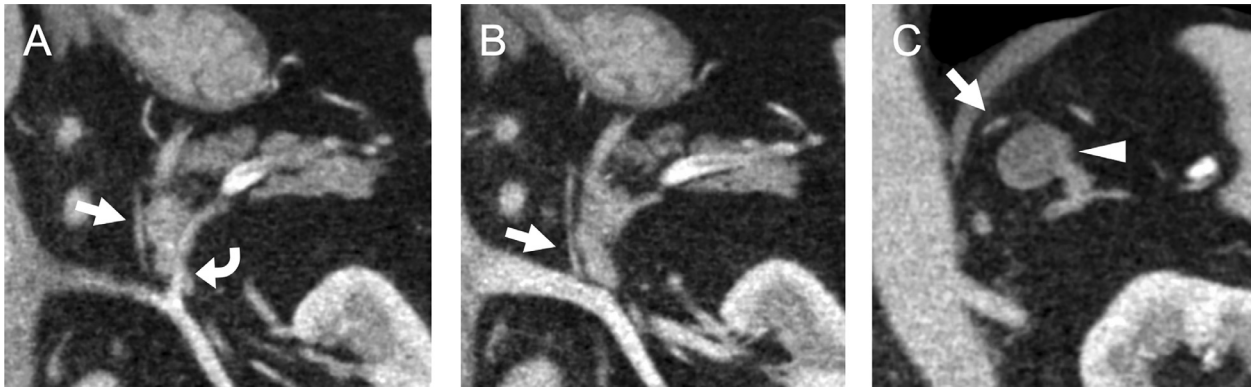

Fig. 1 – Contrast computed tomography images of the left adrenal gland in the coronal view
The left inferior phrenic vein (LIPV, arrow) and left adrenal central vein (curved arrow) separately enter the left renal vein. The left adrenocortical adenoma (arrowhead) is at the cranial apex of the adrenal gland, with the LIPV running nearby.

the outflow tract of adrenal venous blood, which might have influenced the AVS diagnosis.

Ethics committee approval was not required and waived for a case report.

Case presentation

A 60-year-old woman had been treated for hypertension for 10 years. She had a history of asthma. At the age of 58, a left adrenal mass was detected during a physical checkup and on the subsequent computed tomography (CT) scan. A closer endocrinological examination revealed PA with hypokalemia. Adrenocorticotropic hormone (ACTH)-stimulated AVS was performed for subtyping, but the right AVS was unsuccessful. She was referred to our hospital for further investigation.

On physical examination, her blood pressure was 151/98 mm Hg and heart rate was 74 bpm under medications with 40 mg of nifedipine and 1,800 mg of potassium chloride daily. Laboratory tests revealed hypokalemia (2.5 mmol/L), a high plasma aldosterone concentration (PAC; 257 pg/mL), low plasma renin activity (<0.2 ng/mL/h), and high aldosterone-to-renin ratio (at least 1,285) which suggested PA. The captopril challenge test, saline infusion test, furosemide upright test, and rapid ACTH stimulation test confirmed the diagnosis of PA [1,2]. Subclinical Cushing's disease was negative in a dexamethasone suppression test.

Pre-contrast CT revealed a low-density, well-defined round mass 15 mm in diameter at the cranial apex of the left adrenal gland, and the size was the same as that in the previous year. Contrast CT revealed that the LIPV had not formed a common trunk with the LCV and entered the left renal vein directly. The distal part of the LIPV was running near the mass. (Fig. 1)

ACTH-stimulated segmental AVS (SAVS) was performed as previously described [9]. The bilateral adrenal veins and LIPV were cannulated with a 5-F catheter designed for the right and left adrenal veins (MK adrenal type; Hanaco Medical Co., Ltd., Tokyo, Japan), and a 2-F microcatheter (Gold Crest Co., Ltd., Tokyo, Japan) was inserted coaxially. Blood was collected from the bilateral adrenal central and right external iliac veins before and 15 to 90 minutes after ACTH loading, and from a few adrenal tributary veins after loading. Blood sampling was also performed at the proximal and distal LIPVs, considering the possibility of tumor blood flow into it because the PAC at LCV was not high, 6,450 pg/mL after ACTH stimulation in the previous hospital. The contour of the tumor was delineated on the basis of the mild contrast of the superior medial tributary and distal part of the LIPV, indicating a possible tumor blood inflow. The procedure was completed without complications.

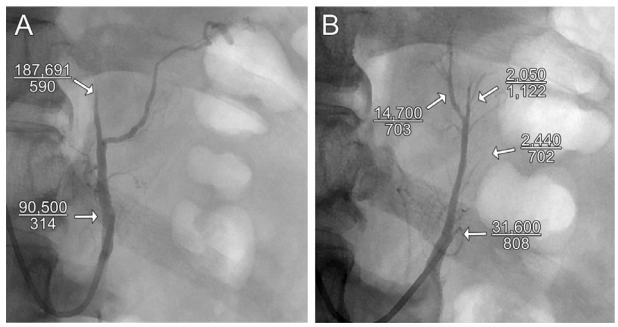

Fig 2 – Venogram of the left inferior phrenic (A) and adrenal central veins (B). The arrows point to the sampling point. The data are the plasma aldosterone concentration (pg/mL)/plasma cortisol concentration (g/dL) after ACTH stimulation.

The blood sampling results are shown in Table 1 and Fig. 2. The findings were as follows: (1) A PAC > 14,000 (pg/mL) after ACTH stimulation was found only on the left side, and the high PAC was consistent with the localization of the adrenal mass. High levels were found in the distal and proximal LIPVs, LCV, and superior medial tributary, in this order, but not in the other tributaries [1,9,10]; (2) The lateralization index (LI), aldosterone-to-cortisol (A/C) ratio on the dominant side over the contralateral side, were 6.8 and 8.5 before and after ACTH stimulation. These values are higher than the com-

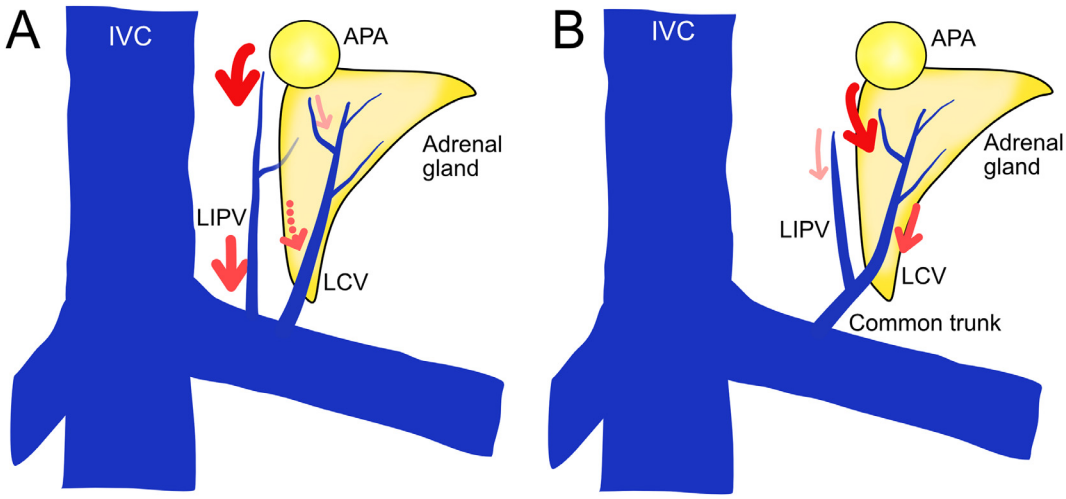

Fig 3 – Schema of the left aldosterone-producing adenoma blood flow in the present case and in a normal case
In the present case (A), much of the aldosterone producing adenoma (APA) blood flowed through the independent left inferior phrenic vein (LIPV) from the left adrenal central vein (LCV). Only a minor outflow was observed into the superior medial tributary, close to the tumor, and probably into the LCV via the superficial veins or fine tributaries. In normal cases (B), the LIPV joins the LCV to form a common trunk. Tumor blood from APA often drains into the LCV via a tributary vein, and flow into the LIPV is minor, if present at all.

Table 1 – Hormone Concentrations in Each Blood Sampling Site before and after ACTH stimulation.

Sampling point	PAC (pg/mL)	PCC (μg/dL)	A/C
Before ACTH stimulation			
Left adrenal central vein	4,870	21.5	227
Right adrenal central vein	504	15.1	33.4
Right external iliac vein	317	12	26.4
After ACTH stimulation			
Left			
Adrenal central vein	31,600	808	39.1
Superior medial tributary	14,700	703	20.9
Superior tributary	2440	702	3.5
Lateral tributary	2050	1,122	1.8
Inferior phrenic vein			
distal	187,691	590	318
proximal	90,500	314	288
Right			
Adrenal central vein	5,030	1,090	4.6
Lateral tributary	2,600	817	3.2
Inferior tributary	3,470	1256	2.8
Right external iliac vein	1,230	39.2	31.4

monly used cutoffs in the conventional AVS, respectively [1,2]; (3) Right adrenal aldosterone secretion was suppressed because the contralateral A/C ratio on the non-dominant side over the right external iliac vein was 0.15 after ACTH stimulation [2]. Therefore, the diagnosis based on the SAVS was left unilateral aldosterone hypersecretion due to a left APA, an indication for surgery.

The PAC and A/C ratio (187,691 pg/mL and 318, respectively) were much higher in the distal LIPV than in the LCV (31,600 pg/mL and 39.1, respectively). The LI calculated with the distal LIPV instead of the common trunk was 68.9 after ACTH stimulation. These findings reinforced the diagnosis.

Subsequently, a left partial adrenalectomy was performed. Immunohistochemistry revealed an adrenocortical adenoma with a Weiss score of 0 and CYP11B2 positivity. The patient's blood pressure was improved to 135/75 mm Hg after 1 year after surgery without antihypertensive medication. Hypokalemia was also cured.

Conclusion

The present patient had a rare venous anomaly in which the LIPV and LCV entered the left renal vein separately. Blood sampling from the LIPV revealed a much higher PAC and A/C ratio from the left APA than from the LCV or tributaries. The schema of the assumed outflow tract of the left APA blood is shown in Fig. 3. It was likely that sampling from the LCV alone would have been indicated surgery considering the calculated LI, but the higher concentrations in the LIPV were more indicative of the need for surgery. This case provides some insights into the adrenal hormone outflow pathway and AVS diagnosis.

Anatomically, the adrenal gland has numerous surrounding venous networks in addition to intra-adrenal veins [11]. The confluence of the left superior adrenal vein, one of the extraglandular adrenal veins, with the LIPV or, rarely, the left adrenal vein was reported to be 37.6% [12]. The anastomosis is frequently depicted on AVS venography [8]. It is considered to act as a collateral blood pathway [13]. In the diagnosis of AVS, the tumor blood flow into these pathways and its impact have not been major issues. Hormone concentrations in the common trunk were usually lower than those in the LCV by dilution with LIPV blood [14]. However, those in the LIPV were sometimes high as in the present case, and blood samples from the LIPV or common trunk may be more useful than samples from LCV, or even trib-

utaries, in demonstrating hormone overproduction in some cases.

Normally, the LIPV joins the LCV to form a common trunk, but reports have described anomalies in which the LIPV and LCV enter the left renal vein independently without forming a common trunk [4-6]. The exact frequency is unknown but is thought to be probably < 1% [7,8]. If a common trunk exists, sampling from the common trunk containing LIPV blood may be sufficient without sampling from the LIPV. However, no common trunk exists, as in the case, the LIPV blood must be collected directly in the vein.

The recommended location of left adrenal vein sampling is different between guidelines, with the common trunk in confluence with the LIPV and LCV preferred in the Endocrine Society Clinical Guidelines and the LCV preferred in the Japan Endocrine Society Guideline [1,2]. Although hormone concentrations are usually diluted in the former, a report showed no significant difference in A/C ratio between the two [14]. However, differences in treatment strategies and false-negative results for APA depending on the left sampling site have been reported [15]. High PAC and A/C ratio in the LIPV as in the present case can lead to higher PAC and A/C ratio in the common trunk than in the LCV in a normal adrenal vein anatomy, which explains one of the causes of the different subtyping. For instance, the higher LI in the common trunk is determined to be a left unilateral lesion; and the lower LI in the LCV, a bilateral lesion.

In addition, the PAC and A/C ratios were higher in the LCV than in the collected prominent tributaries, suggesting that the APA blood flowed into the LCV through the superficial or fine tributary veins not sampled. Even within the LCV, between the prominent tributary and common trunk, hormone concentrations might be different depending on proximal or distal position, possibly suggesting a potential impact on the diagnosis.

On CT, the left adrenal mass was at the cranial apex, and the distal part of the LIPV ran near the mass. In this situation, blood sampling in this location may be more important.

This report has some considerable limitations. First, whether ACTH stimulation should be used in AVS remains controversial. Second, the fact that it was the second AVS may have influenced the results, although CT and venography revealed no apparent abnormalities such as hemorrhage or vascular injuries.

In conclusion, blood sampling in the LIPV could be important in AVS diagnosis because the LIPV is rarely not confluent with the LCV or might show high aldosterone level from APA.

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