

Editorial Comment

Adrenal Venous Sampling Is Absolutely Requisite for Definitively Diagnosing Primary Aldosteronism as Well as for Detecting Laterality of the Adrenal Lesion

Tetsuo NISHIKAWA¹⁾, Jun SAITO¹⁾, and Masao OMURA²⁾

(*Hypertens Res* 2007; 30: 1009–1010)

Key Words: primary aldosteronism, aldosterone-producing adenoma, idiopathic hyperaldosteronism, adrenal venous sampling

Primary aldosteronism (PA) is a curable form of secondary hypertension, and recent studies (1–6) indicate that the incidence of PA among hypertensives is higher than previously reported. We previously reported that a diagnosis of PA was made in around 6% of the 1,020 hypertensive patients we treated between 1995 and 1999, suggesting that PA is common among hypertensive patients (7, 8). Recent evidence suggests that aldosterone excess may have specific cardiotoxicity that is reversible with treatment. Thus, it is important to accurately diagnose PA in these patients and to treat PA as soon as possible. The two major subtypes of primary aldosteronism are unilateral aldosterone-producing adenoma (APA) and bilateral idiopathic hyperplasia (IHA). APA typically responds to unilateral adrenalectomy, which corrects hyperaldosteronemia and can attenuate hypertension. The medical management of IHA is generally recommended (9–12), since unilateral or subtotal adrenalectomy results in only 15–20% cure rates for hypertension (9, 13). Therefore, distinguishing APA from IHA is critical for deciding on the type of treatment.

In the present issue of *Hypertension Research*, Satoh *et al.* (14) report on the importance of adrenal vein sampling (AVS), which requires a unique and elegant method to detect laterality of adrenal disorders in primary aldosteronism. The authors retrospectively studied 87 cases of PA examined by

AVS (14). Their AVS methods are quite new and this is the first time they have been reported. They collected right and left adrenal venous effluents simultaneously before and after adrenocorticotrophic hormone (ACTH) stimulation for measurements of aldosterone (A) and cortisol concentrations (C). Based on the AVS results, the receiver operator characteristics (ROC) curve analysis between the operated group and the group without apparent laterality demonstrated that the A/C ratio of the higher side to that of the lower side (A/C ratio) after ACTH stimulation is a useful index with a cut-off value of 2.6, a sensitivity of 0.98 and a specificity of 1.0. The ROC curve analysis between the APA side and the contralateral side within surgically treated patients demonstrated that the cut-off value of aldosterone concentration is 1,340 ng/dL with a sensitivity of 0.92 and a specificity of 1.00. Based on these findings, the authors emphasized the usefulness of simultaneous AVS and ACTH stimulation for localizing APA.

Based on our studies of AVS performed individually to obtain blood first from the right and then from the left adrenal, we judged that the catheters had been correctly inserted into the adrenal vein when cortisol concentration levels in the adrenal venous effluents were more than 40 µg/dL before ACTH treatment and more than 200 µg/dL 30 min after stimulation (8, 15, 16). We then made a diagnosis of aldosterone hypersecretion when aldosterone concentrations in the adre-

From the ¹⁾Division of Endocrinology and Metabolism, Department of Medicine and ²⁾Department of Medical Examination, Yokohama Rosai Hospital, Yokohama, Japan.

Address for Reprints: Tetsuo Nishikawa, M.D., Ph.D., Division of Endocrinology and Metabolism, Department of Medicine, Yokohama Rosai Hospital, 3211 Kozukue-cho, Kohoku-ku, Yokohama 222–0036, Japan. E-mail: tetsuon@yokohamah.rofuku.go.jp

Received July 31, 2007.

nal venous effluents were more than 250 ng/dL before ACTH treatment and more than 1,400 ng/dL 30 min after stimulation. Tiny lesions such as aldosterone-producing microadenoma (APmicroA), unilateral adrenal hyperplasia (UAH) (17) and unilateral multiple micronodules (UMN) (15) have been diagnosed by ACTH-AVS. We have been performing ACTH-AVS since 1994 to distinguish between unilateral and bilateral hypersecretion of A. Using this method, we have been able to adequately diagnose APmicroAs, which are impossible to detect by CT.

There is a limitation in the ability of CT to differentiate APA from IHA, because the size of APA is usually so small that CT images cannot consistently detect the lesions (7, 8, 15, 16). In evaluating whether the lesion involves the unilateral or bilateral adrenal glands, diagnostic imaging of the adrenal glands is less accurate, and microlesions may frequently be missed, resulting in a diagnosis of IHA. In the diagnosis of PA, localization should be accurately evaluated in order to select appropriate therapeutic strategies, such as unilateral adrenalectomy and drug treatment. AVS is essential to establish the correct diagnosis of PA (18–21).

The data of Satoh *et al.* (14) clearly demonstrate the importance of AVS for detecting laterality in patients with PA, although AVS is considered a quite difficult examination technique for many radiologists. Moreover, they apparently suggest cut-off values for evaluation of the sampling data, using the absolute value of aldosterone concentration and the ratio of A to C in selective sampling. These data are helpful for correctly diagnosing PA and should be used as standard criteria for AVS.

References

- Gordon RD, Stowasser M, Tunny TJ, Klemm SA, Rutherford JC: High incidence of primary aldosteronism in 199 patients referred with hypertension. *Clin Exp Pharmacol Physiol* 1994; **21**: 315–318.
- Komiya I, Yamada T, Takasu N, *et al*: An abnormal sodium metabolism in Japanese patients with essential hypertension, judged by serum sodium distribution, renal function and the renin-aldosterone system. *J Hypertens* 1997; **15**: 65–72.
- Lim PO, Dow E, Brennan G, Jung RT, MacDonald TM: High prevalence of primary aldosteronism in the Tayside hypertension clinic population. *J Hum Hypertens* 2000; **14**: 311–315.
- Fardella CE, Mosso L, Gómez-Sánchez C, *et al*: Primary hyperaldosteronism in essential hypertensives: prevalence, biochemical profile, and molecular biology. *J Clin Endocrinol Metab* 2000; **85**: 1863–1867.
- Loh KC, Koay ES, Khaw MC, Emmanuel SC, Young WF Jr: Prevalence of primary aldosteronism among Asian hypertensive patients in Singapore. *J Clin Endocrinol Metab* 2000; **85**: 2854–2859.
- Rossi E, Regolisti G, Negro A, Sani C, Davoli S, Perazzoli F: High prevalence of primary aldosteronism using postcaptopril plasma aldosterone to renin ratio as a screening test among Italian hypertensives. *Am J Hypertens* 2002; **15**: 896–902.
- Nishikawa T, Omura M: Clinical characteristics of primary aldosteronism: its prevalence and comparative studies on various causes of primary aldosteronism in Yokohama Rosai Hospital. *Biomed Pharmacother* 2000; **54** (Suppl 1): 83s–85s.
- 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.
- Weinberger MH, Grim CE, Hollifield JW, *et al*: Primary aldosteronism. *Ann Intern Med* 1979; **90**: 386–395.
- Ganguly A: Primary aldosteronism. *New Engl J Med* 1998; **339**: 1828–1834.
- Stewart PM: Mineralocorticoid hypertension. *Lancet* 1999; **353**: 1341–1347.
- Lim PO, Young WF, MacDonald TM: A review of the medical treatment of primary aldosteronism. *J Hypertens* 2001; **19**: 353–361.
- Banks WA, Kastin AJ, Biglieri EG, Ruiz AE: Primary adrenal hyperplasia: a new subset of primary hyperaldosteronism. *J Clin Endocrinol Metab* 1984; **58**: 783–785.
- Satoh F, Abe T, Tanemoto M, *et al*: Localization of aldosterone producing adrenocortical adenomas: significance of adrenal venous sampling. *Hypertens Res* 2007; **30**: 1083–1095.
- Omura M, Sasano H, Fujiwara T, Yamaguchi K, Nishikawa T: Unique cases of unilateral hyperaldosteronism due to multiple adrenocortical micronodules, which can only be detected by selected adrenal venous sampling. *Metabolism* 2002; **51**: 350–355.
- Omura M, Sasano H, Saito J, Yamaguchi K, Kakuta Y, Nishikawa T: Clinical characteristics of aldosterone-producing microadenoma, macroadenoma, and idiopathic hyperaldosteronism in 93 patients with primary aldosteronism. *Hypertens Res* 2006; **29**: 883–889.
- Ross EJ: Conn's syndrome due to adrenal hyperplasia with hypertrophy of zona glomerulosa, relieved by unilateral adrenalectomy. *Am J Med* 1965; **39**: 994–1002.
- Radin DR, Manoogian C, Nadler JL: Diagnosis of primary aldosteronism: importance of correlating CT findings with endocrinological studies. *Am J Roentgenol* 1992; **158**: 553–557.
- Young WF Jr: Primary aldosteronism: a common and curable form of hypertension. *Cardiol Rev* 1999; **7**: 207–214.
- Harper R, Ferrett CG, McKnight JA, *et al*: Accuracy of CT scanning and adrenal vein sampling in the pre-operative localization of aldosterone-secreting adrenal adenomas. *QJM* 1999; **92**: 643–650.
- Magill SB, Raff H, Shaker JL, *et al*: Comparison of adrenal vein sampling and computed tomography in the differentiation of primary aldosteronism. *J Clin Endocrinol Metab* 2001; **86**: 1066–1071.