Bilateral Adrenal Nodules: Which Side is Functioning?

A 73-year-old male visited the Emergency Department for weakness in both legs. He had a 20-year history of hypertension. At the Emergency Department, his blood pressure was high (160/100 mmHg). Routine laboratory tests revealed hypokalemia (serum potassium level, 1.9 mEq/L). Additional laboratory tests were done and his aldosterone-renin ratio was 80.9 (serum aldosterone, 28.3 ng/dL; plasma renin activity, 0.35 ng/mL/h), which suggested primary aldosteronism (PA). Suppression tests confirmed the diagnosis; his serum aldosterone remained elevated after acute saline loading with intravenous saline (33.8 ng/dL).

On abdominopelvic computed tomography (CT), bilateral adrenal nodules (right, 1.7 cm; left side, 1 cm) were detected (Fig. 1). To determine which side was functioning, bilateral adrenal venous sampling (AVS) was done, but the sampling failed to determine lateralization because it was not performed at the correct position. Therefore, we performed adrenal cortical imaging using radioiodinated I-6-β-iodomethyl-19-norcholesterol (NP-59) with single photon emission computed tomography-computed tomography (SPECT-CT) (Fig. 2). To block thyroid uptake of the free form of radioactive iodine, 10 drops of Lugol solution were given daily (for 1 week, beginning 2 days before NP-59 injection). Pharmacological adrenosuppression, dexamethasone was given orally (1 mg four times a day starting 7 days before NP-59 injection and continuing until the last day of scanning). After these two preparations, Iodine-131 (I-131) NP-59 was injected intravenously. Planar NP-59 abdominal images taken on day 3 demonstrated asymmetric and focal uptake in the region of the 1.7-cm-sized nodule in the right adrenal gland, which persisted on images taken on day 6 (Fig. 2A, C). NP-59 SPECT-CT confirmed that the right adrenal nodule was functional and was responsible for the patient's laboratory results (Fig. 2B, D). Laparoscopic adrenalectomy of the right adrenal gland was performed and the pathologic result was adrenocortical adenoma. Laparoscopic adrenalectomy was performed via the retroperitoneal approach. The patient was placed in the full flank position on the operating table. After trocar insertion, the Gerota's fascia was opened, and the upper pole of the kidney was mobilized to expose the adrenal gland. The adrenal vein was ligated from the inferior vena cava. Then the adrenal gland was dissected off the surrounding organs. Because the patient's blood pressure was well controlled by medication, we did not use any drugs for aldosteronism. Total operative time was 115 minutes and transfusion was not needed. After the adrenalectomy, his laboratory results including potassium and aldosterone became normalized.
FIG. 1. (A, B) Abdominopelvic computed tomography showed bilateral adrenal nodules (arrows).

FIG. 2. Iodine-131 I-6-β-iodomethyl-19-norcholesterol (NP-59) scintigraphy showed hot uptake in the right adrenal nodule. After intravenous injection of NP-59, focal hot uptake (arrows) was shown in the right adrenal nodule on the images taken on the 3rd (A, B) and 6th days (C, D) (A and C, posterior planar images of lower back; B and D, single photon emission computed tomography-computed tomography).
Bilateral Adrenal Nodules With Primary Aldosterone

Schteingart [1] reported that 60% of cases of PA are secondary to bilateral adrenocortical hyperplasia. It is known that patients with PA secondary to adenoma usually have hypertension and hypokalemia, as in this case, and they can be cured with unilateral laparoscopic adrenalectomy [1]. In contrast, patients with PA secondary to hyperplasia may show milder clinical manifestations and may not benefit from this surgery, with PA reappearing shortly after the operation [1,2].

Adrenal Venous Sampling

AVS is the gold standard in localization of the source of autonomous aldosterone but it is invasive and technically challenging [3,4]. For comparison, the bilateral adrenal vein must be sampled. However, the right adrenal vein enters the inferior vena cava at an acute angle, resulting in inappropriate cannulation. Vonend et al. [4] reported that the success rate of AVS was so variable that centers completing less than 20 procedures had success rates of 8% to 10% and that even specialized centers had poor success rates. When the result is inconclusive after AVS, NP-59 scintigraphy can be done [5].

Adrenal Cortical Imaging With I-131 NP-59 SPECT-CT

The radiolabeled cholesterol analogue I-131 NP-59 is the tracer bound to low-density lipoproteins and is esterified and stored without further metabolism in adrenocortical cells [6]. It can be used in hypersecretory adrenocortical disease such as hypercortisolism, hyperaldosteronism, or hyperandrogenism [6]. Thyroid blockade with saturated potassium iodine or Lugol solution is needed. Dexamethasone suppression is needed to suppress the radio-pharmaceutical uptake to the normal adrenal gland. Dexamethasone is given orally by the methods described earlier in this case. Scanning can be done at 3 to 5 days after intravenous injection of I-131 NP-59. Additional scanning can be done around day 7. Unilateral uptake on early images indicates unilateral adenoma or unilateral hyperplasia. Symmetrical uptakes on early images suggest bilateral autonomous hyperplasia [7].

The NP-59 scintigraphy in this case with bilateral adrenal nodules showed focal uptake in the right adrenal gland only (Figs. 1, 2), aiding in lateralization for adrenalectomy. Moreover, SPECT-CT confirmed that the uptake was in the right adrenal gland. Application of SPECT-CT is known to show superior diagnostic accuracy with NP-59 with a sensitivity of 81.8% compared with planar-only imaging (sensitivity, 40.9%) [5]. Lombardi et al. [7] reported that noninvasive adrenal imaging with CT and NP-59 scintigraphy shows such high accuracy and sensitivity that AVS should be indicated only when noninvasive imaging is not conclusive.

In conclusion, this is an educational case with bilateral adrenal nodules with hyperaldosteronism with inconclusive results of AVS. Adrenalectomy based on lateralization of NP-59 scintigraphy was helpful.

CONFLICTS OF INTEREST
The authors have nothing to disclose.

REFERENCES

1. Schteingart DE. The clinical spectrum of adrenocortical hyperplasia. Curr Opin Endocrinol Diabetes Obes 2012;19:176-82.
2. Douma S, Petidis K, Kamparoudis A, Gkaliagkousi E, Anyfanti P, Doumas M, et al. Surgical management of primary aldosteronism. not everything that shines is gold. Clin Exp Hypertens 2012;34:53-6.
3. Bouhanick B, Delchier MC, Fauvel J, Rousseau H, Amar J, Chamontin B. Is it useful to repeat an adrenal venous sampling in patients with primary hyperaldosteronism? Ann Cardiol Angeiol (Paris) 2014;63:23-7.
4. Vonend O, Ockenfels N, Gao X, Alloio B, Lang K, Mai K, et al. Adrenal venous sampling: evaluation of the German Conn’s Registry. Hypertension 2011;57:990-5.
5. Yen RF, Wu VC, Liu KL, Cheng MF, Wu YW, Chueh SC, et al. 131I-6beta-iodomethyl-19-norcholesterol SPECT/CT for primary aldosteronism patients with inconclusive adrenal venous sampling and CT results. J Nucl Med 2009;50:1631-7.
6. Kurtaran A, Traub T, Shapiro B. Scintigraphic imaging of the adrenal glands. Eur J Radiol 2002;41:123-30.
7. Lombardi CP, Raffaeli M, De Crea C, Rufini V, Treglia G, Bellantone R. Noninvasive adrenal imaging in hyperaldosteronism: is it accurate for correctly identifying patients who should be selected for surgery? Langenbecks Arch Surg 2007;392:623-8.