Ultrasonography in the Diagnosis of Aldosterone-Producing Adenoma: Is It Useful?

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The usefulness of ultrasonography (US) in the diagnosis of aldosterone-producing adenoma(s) (APA) was compared with computed tomography (CT) and adrenal scintigraphy in 13 patients. The initial examination with US could demonstrate four of seven right APA. Repeat examinations later in two patients whose tumors were initially not detectable did reveal a tumor in one patient. On the other hand, two left APA were delineated on the initial trial. The other seven left APA, except two small APA in one patient, could be delineated during repeat US examinations performed on other days. With CT, all APA were detected during the first or second trial except for the smallest one. The rate of localization by adrenal scintigraphy with dexamethasone pretreatment was 11 of 13 patients. CT had the highest localization rate. However, US was shown to be useful in the localization diagnosis of APA on repeat examinations with a high delineation rate comparable to CT.

Key words: primary aldosteronism, aldosteronoma, image diagnosis

Introduction

Computed axial tomography (CT) is generally considered to be superior to ultrasonography (US) in the localization diagnosis of small adrenal tumors (1-3). However, in Japan, there has recently been an increase in the use of CT, so that a patient must wait one to two weeks before examination. This specialized apparatus requires a trained technician for its operation. In contrast, due to the wide availability of US, its non-invasiveness and simplicity of operation this modality has been proven to be very useful for clinicians. Repeat examinations can be done immediately as early as one desires. However, the usefulness of US to detect small adrenal tumors remains controversial (1-5). Recently, this problem has been offset with the improvement in resolution, thereby increasing the detection rate even for small adrenal tumors (3, 4, 6, 7).

Most aldosterone-producing adenomas (APA) are too small to be detected incidentally by imaging procedures (8, 9). Usually the presence of APA is suspected only after a routine endocrine work-up showing some results suggestive of primary aldosteronism. The purpose of this study was to clarify whether US is useful in the diagnosis of APA when its advantageous characteristics are fully utilized, and to compare it with CT and adrenal scintigraphy.

Materials and Methods

Thirteen patients (5 males, 8 females) who were admitted for hypertension, hypokalemia, and hyporeninemic hyperaldosteronism were selected for the study. All examinations were performed after obtaining informed consent. Their body weight was within the range of ±20% of ideal body weight calculated by Hirata’s method (10). Plasma renin activity in all of the patients was suppressed even after the renin provocation tests. The presence of APA was surgically confirmed in all cases. Eleven patients (Cases 2-12) had only one APA. Cases 1 and 13, however, had two right and three left APA, respectively. The maximal diameter of resected tumors was 6-28 mm as shown in Table 1.

Imaging examinations were made after performing the renin provocation tests. Examinations with US were performed by a single physician (NY) throughout the study. Initial US examinations were performed before CT examinations in all patients. A 3.5 MHz real-time linear-sector-scanner YGM RT-3,600® (Yokogawa Medical System, Tokyo) was used as previously reported (11). In the patients whose adrenal lesions could not be depicted during the initial examination, re-examination with the same methods was performed before the initial CT in Cases 9, 11, 12, and 13 and a few days after the initial CT in Cases 5, 6 and 10.

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A single tumor was made, which on surgery showed two masses in the right adrenal gland; that is, a smaller tumor (12 mm in diameter) was missed. In two patients with right APA (Cases 5 and 6) which were not demonstrated initially by US, the lesions could not be demonstrated on repeat examination. In one patient (Case 6), however, APA was demonstrated by US 2 years later, while it was not demonstrated 6 months later in the other (Case 5). The size was 8 mm in Case 5 and 17 mm in Case 6.

As far as the left APA is concerned, the tumors were delineated only in two (Cases 7 and 8) of seven patients during the initial examination. The diameter of the delineated tumors was 20 mm in Case 7 and 15 mm in Case 8. However, localization diagnosis of the left APA by repeat US was well-facilitated in 5 patients with a mean tumor diameter of 17 ± 3 mm (Cases 9–13). In one patient (Case 13) who had three left APA, US did not demonstrate the two smaller tumors, being 10 and 6 mm in size.

2) CT examination

In four (Cases 1–4) of six patients with right APA, adrenal tumors were demonstrated at the initial examination. Even the two right APA found during surgery in one patient (Case 1) had been accurately demonstrated by CT. The mean size of the right APA demonstrated by the initial CT was 16 ± 8 mm in diameter. In two patients (Cases 5 and 6) whose APA was not demonstrated by the initial CT as well as US, APA were depicted by CT 6 months and 2 years later in Cases 5 and 11, respectively.

In all seven patients with left APA, a tumor image could be detected at the initial examination. The size of the demonstrable left APA was 16 ± 4 mm. However, in the patient having three left APA (Case 13), the three tumors were delineated as two tumors. The undetected APA in Case 13 had the smallest diameter (6 mm) among all the tumors.

3) Adrenal scintigraphy

Adrenal scintigram without dexamethasone pretreatment showed a higher uptake on the tumor side in seven of nine patients examined. With dexamethasone pretreatment, uptake only in the tumor side was seen in 11 of 13 patients. Bilateral uptake was seen in the remaining two patients (Table 1).

**Discussion**

It is occasionally difficult to diagnose primary aldosteronism solely by clinical signs and biochemical investigation. Imaging examinations are imperative not only in the differential diagnosis of primary aldosteronism due to APA and idiopathic hyperaldosteronism but also in tumor localization. Although CT, adrenal scintigraphy (12, 13) and adrenal venous sampling (2, 14, 15) have been reported to be useful for the localization of APA, these procedures have some limitations. In a survey

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R: right, L: left, +: demonstrated by the initial examination, (+) not delineated by the initial examination, but demonstrated by repeat examination on another day, −: not delineated, Scinti: adrenal scintigraphy, Dex(−) or Dex(+): without or with dexamethasone pretreatment, # demonstrated 2 years after the initial attempt, § in cases 5 and 6, demonstrated by re-examination 6 months and 2 years later, respectively, > = < indicating the intensity of the uptake, RU or LU: only right or left adrenal uptake, BU: bilateral adrenal uptake, NE: not examined.

CT instruments were GE CT/T 8,800® (General Electric Co., Milwaukee) or YGM QUANTEX® (Yokogawa Medical System). Slice thickness and slice-center distance were both 5 mm. Matrix number was 256 × 256.

US and CT were performed early in the morning following an overnight fast without premedication. In two patients (Cases 5 and 6) whose APA could not be demonstrated either by US or CT during the first admission, re-examinations were done 6 months and 2 years later, respectively.

Adrenal scintigraphy was performed 3 to 7 days after the intravenous injection of 1 mCi of 131I-NCL6 (Adosterol®, Daiichi Radioisotope, Tokyo) without and/or with pretreatment with dexamethasone (3 mg daily) given for 7 days. Adrenal scintigraphy was performed after US and CT examinations.

**Results**

1) US examinations

In six patients with right APA, four APA (Cases 1–4), whose mean maximal diameter was 17 ± 9 mm (±MSD), could be demonstrated during the initial examination. However, in one patient (Case 1) an initial diagnosis of a single tumor was made, which on surgery showed two
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study (16) the majority (87%) of APA were less than 2.5 cm in diameter, and the adrenal glands are located deep within the rib-cage in the retroperitoneal fatty tissue. Delineation of small adrenal tumors by US is therefore not easy (1, 5). However, Yeh (7) reported that adrenal masses as small as 6 mm can be detected by US. A similar report by Günther et al (4) described that US demonstrated 12 of 13 small adrenal masses 8 to 20 mm in diameter.

The delineation rate by initial CT examination in this series, especially for the left APA, was superior to US. APA in this study were small, ranging from 6 to 28 mm, although none of the patients were obese. The tumor size of those not depicted by US was 8 (Case 5) and 12 mm (Case 1) on the right side, and 6 and 10 mm (both; Case 13) on the left. These tumors were smaller than those depicted by US, with a mean size of 17 mm in the respective sides. On the other hand, CT demonstrated all tumors except for the smallest one with a diameter of 6 mm (Case 13). The superiority of CT to US in the demonstration of adrenal tumor is generally accepted (1, 5). This contradicts the contention of Sample and Sarti (17), however, who reported a rather superior delineation rate of US to that of CT. The present results suggest that US may not be useful to detect left APA, if only a single attempt is performed, and may overlook the small APA of 10 mm or less in diameter.

Five APA were delineated in seven patients (Cases 5, 6, 9–13) who had a repeat US examination. In one patient (Case 10), CT findings were known by the operator when the second US was performed, which could have influenced the performance of the repeat US test. However, this possibility is not conceivable at least in the other four patients (Cases 9, 11, 12 and 13), since US depicted the tumor before the CT findings were obtained. The delineation of the left adrenal lesion by US largely depends on the condition of the gastrointestinal gas as previously reported (11), which causes a lower delineation rate of the left APA on the initial investigation. It is probable that the patient condition on the second attempt was better than that on the initial examination, since no further pretreatment other than overnight-fasting was administered for both examinations. According to our experience for a few non-hyperfunctioning adrenal adenomas on the left side, filling the stomach with boiled water had no effect on the abdominal gas which could disturb the delineation of the tumors by US (data not shown). Bowel gas may be more critical than stomach gas in decreasing the delineation rate of left adrenal tumor. Some pretreatment being used to decrease bowel gas may improve the final delineation rate of left APA. Such pretreatments, however, may be inconvenient for both the clinician and patient, and likewise might be disadvantageous for the performance of US examination. From these results, it is suggested to emphasize the necessity of re-examination of US when no tumor is depicted.

Although the rate of localization by scintigraphy was high in this series, there is an exposure to radiation (18), like adrenal venous sampling, and it is expensive. CT showed the highest localization rate on first attempt while US showed a high detection rate comparable to CT, as far as the right APA was concerned. US is still clinically useful for the detection of APA larger than about 10 mm in diameter, although it requires careful and repeated scanning. The possibility that US may detect the tumor by repeated examinations while a patient is waiting for his scheduled CT examination may lessen the time of work-up.

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References

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