The role of adrenocortical scintigraphy in the evaluation of unilateral incidentally discovered adrenal and juxtaadrenal masses

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We reviewed the findings of adrenocortical scintigraphy with ^{131}I-6-beta-iodomethyl-19-norcholesterol (NCL-6-^{131}I) of 39 patients to clarify its role in the evaluation of unilateral adrenal or juxtaadrenal masses incidentally discovered by CT, ultrasonography or plain radiography. Twenty-seven benign adrenal masses showed various scintigraphic findings (hot nodule: 12 silent adenomas, warm nodule: one solid mass, normal appearance: one cyst and 2 solid masses, diffuse decrease: each one; solid mass, myelolipoma, ganglioneuroma and calcified adrenal and partial or complete defect: each one; solid mass, myelolipoma and ganglioneuroma and 2 cysts and 2 pheochromocytomas); while a partial or complete defect was shown in a nonfunctioning carcinoma and 3 metastases and a complete defect or inhomogeneous uptake without opposite adrenal visualization was shown in 2 patients with cortisol-producing carcinoma. Therefore a hot nodule and an inhomogenous uptake or complete defect with nonvisualization of the opposite adrenal are specific to a benign tumor and a cortisol-producing carcinoma, respectively. The impaired tumor uptake of NCL-6-^{131}I is a nonspecific finding. The scintigraphic findings of juxtaadrenal masses were normal in 4 and deviated adrenals in 2. Thus adrenocortical scintigraphy can identify silent adenomas and cortisol-producing carcinomas among the adrenal masses and may help to differentiate juxtaadrenal from adrenal masses.

Key words: Adrenal gland, adrenocortical scintigraphy, incidentaloma, neoplasm, ^{131}I labelled iodocholesterol.

INTRODUCTION

Adrenal or juxtaadrenal masses have been incidentally and increasingly discovered with the wider spread and application of computed tomography (CT) and ultrasonography (US).[1-3] The cause of these incidental masses may be inferred in some cases by characteristic findings in CT, US and magnetic resonance imaging (MRI).[4-7] However

these diagnostic procedures have limited value in differentiating benign from malignant adrenal masses[6,8-10] and adrenal from juxtaadrenal masses.[3]

The scintigraphic approach, which uses the uptake of the cholesterol analog, ^{131}I-6-beta-iodomethyl-19-norcholesterol(NCL-6-^{131}I[11] or NP-59[12]) into adrenocortical tissues can provide unique functional information about adrenocortical steroid hormone secretion[13,14] and visualize the differential functional status of the adrenal cortex in patients with euadrenal masses.[15-17] In this paper, we reviewed the scintigraphic findings of incidentally discovered unilateral adrenal and juxtaadrenal masses to study the role of adrenocortical scintigraphy in the evaluation of these masses initially discovered with CT, US or abdominal X-ray examination.

PATIENTS AND METHODS

Patients: Adrenocortical scintigraphy was performed in 120 patients in the 5.5 year period from Jan., 1986 to June, 1991. Of these, 43 patients (36%) were referred for study due to a unilateral adrenal or juxtaadrenal mass lesion discovered with CT, US or plain abdominal radiography done for reasons other than suspicion of adrenal disease (in 28 during a diagnostic work-up for the disease of another organ such as the liver or pancreas, in 7 with abdominal or lumbar symptoms, and in 8 with pre- or post-operative malignant extraadrenal neoplasm). The mass was initially discovered by CT in 31 patients, US in 11 and plain radiography in one. Of the 43 patients, 4 were excluded from this study because a final diagnosis could not be obtained due to inadequate examination or follow-up. Blood and/or urine adrenal hormonal measurements and CT were done in all 39 patients. The final diagnosis was proved by means of histological examination in 15 patients and clinical and CT follow-up in 24.

Adrenocortical scintigraphy:[14,18] Thirty-seven MBq of NCL-6-^{131}I was injected intravenously one day after oral administration of 300 mg potassium iodide powder per day for 7 days to suppress thyroidal accumulation of free [131]I. Scintigraphy was performed with a gamma camera 7 days after NCL-6-^{131}I injection. A posterior adrenal image was obtained with a multiparallel hole high-energy collimator to evaluate the difference between the radioactive concentrations in the two adrenals and determine their positions. Then each posterior adrenal image was separately obtained with a pinhole collimator.

Scan interpretation was based on the morphological appearance of the adrenal by comparing with CT findings of the mass. The difference between the radioactive concentrations in the two adrenals was used as additional information. The mass size was expressed as the average of the maximum cross diameters on the CT slice which contained the largest mass size.

RESULTS

The morphological appearances of the adrenals could be divided into a hot nodule only, a hot nodule with adjacent activity, a warm nodule, a large inhomogenous uptake, a normal pattern,[18] a diffuse decrease, a partial defect, a complete defect and deviation (Fig. 1). The difference between the radioactive concentrations in the two glands could be divided into the following four patterns: increased uptake of the tracer on the mass-side adrenal (concordant uptake), decreased uptake on the mass-side
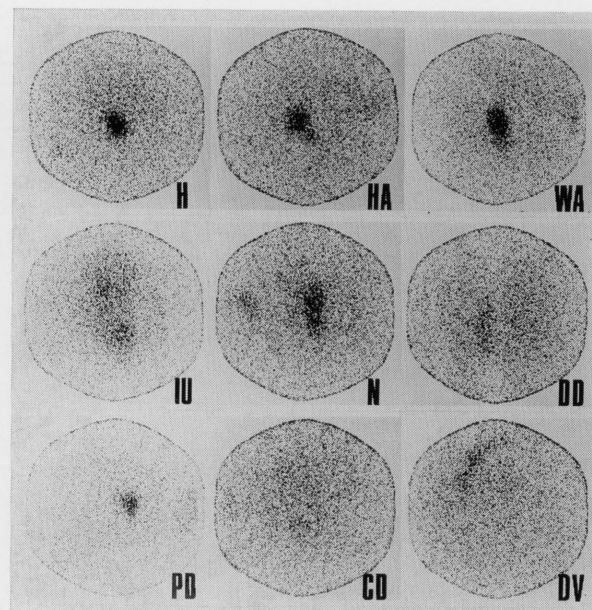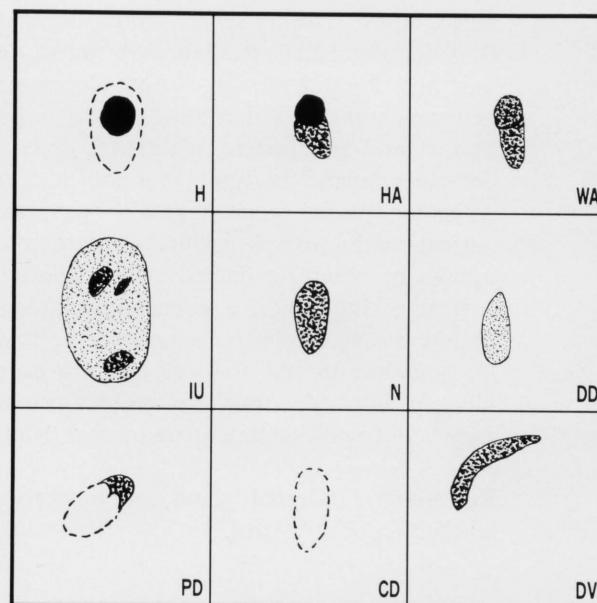
Fig. 1 Adrenocortical imaging findings of the adrenals observed in this study. Representative original images (a) and their schematic presentation (b). H; hot nodule only, HA; hot nodule with adjacent activity, WA; warm nodule, IU: inhomogenous uptake, N; normal pattern, DD; diffuse decrease, PD; partial defect, CD; complete defect and DV; deviation.

adrenal (disconcordant uptake), symmetric uptake and bilateral nonvisualization.

The relationships of adrenal imaging findings to adrenal or juxtaadrenal masses are shown in Table 1.

1. Benign adrenal mass group.
This group consisted of 27 adrenal masses: 16 solid

Table 1 The adrenocortical imaging findings of adrenal and juxtaadrenal masses

| Final diagnosis (Adrenal mass)	H	HA	HA	WA	IU	N	N	N	DD	DD	DD	PD	PD	CD	CD	DV	DV	Total
Tumor side / Opposite side	>CD	>N	>DD	<N >CD	>N >CD	=N	<N	>N	=N	<N	>N	=N	<N	<N	=CD	=N	<N	
Benign mass																		
Solid mass	2	3	6	1	1	1				1				1				16
Cortical adenoma		1(1)																1(1)
Cyst						1							2(1)					3(1)
Myelolipoma								1						1(1)				2(1)
Ganglioneuroma									1(1)					1(1)				2(2)
Pheochromocytoma											1(1)			1(1)				2(2)
Calcified adrenal										1								1
Malignant tumor																		
Cortical carcinoma					1(1)										1(1)			2(2)
Carcinoma														1				1
Metastasis												1	1	1				3
Juxtaadrenal mass																		
Pheochromocytoma							1(1)											1(1)
Renal cell carcinoma							1(1)											1(1)
Retroperitoneal carcinoma						1(1)												1(1)
Neurilemmoma							1(1)											1(1)
Retroperitoneal teratoma																1(1)		1(1)
Renal hematoma																	1(1)	1(1)
Total	2	4(1)	6	1	1(1)	3(1)	3(3)	1	1(1)	2	1(1)	1	3(1)	6(3)	1(1)	1(1)	1(1)	39(15)

* Abbreviations are the same as used in Fig. 1.
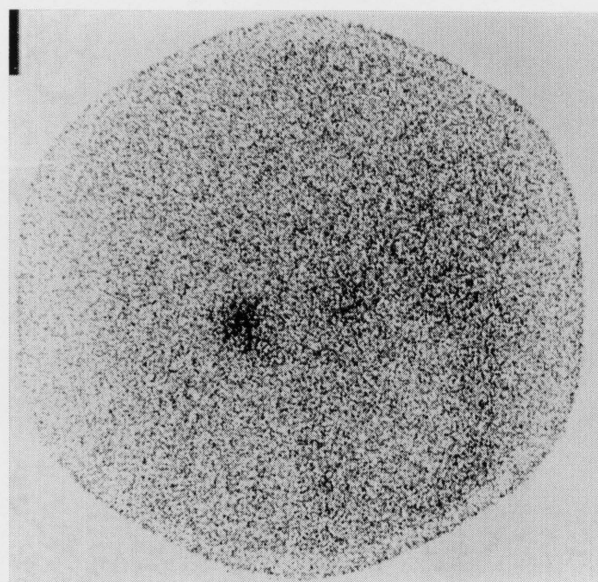>; concordant uptake, <; disconcordant uptake, =; symmetric uptake, CD=CD; bilateral nonvisualization.
Numbers in parentheses give the number of removed masses.

masses on CT scans, one histologically proved cortical adenoma, 3 cysts (one proved by removal; the other 2 had characteristic CT findings), 2 myelolipomas, 2 ganglioneuromas, 2 pheochromocytomas and one calcified adrenal. Seven adrenal masses were diagnosed by histological examination. The remaining 20 adrenal masses showed no change in size with CT follow-up at 6 month to 4-year intervals. Twenty-five patients were euadrenal except 2 with pheochromocytoma. A hot nodule with or without adjacent activity was observed in 12 patients. These were 7 left and 5 right adrenal masses (male: female = 6: 6, age range: 48–68 years). All the hot nodules were solid and ranged from 1.0 to 2.5 cm (mean ± SD: 1.8 ± 0.6 cm) in diameter on CT scans. One of these masses was proved to be adrenocortical
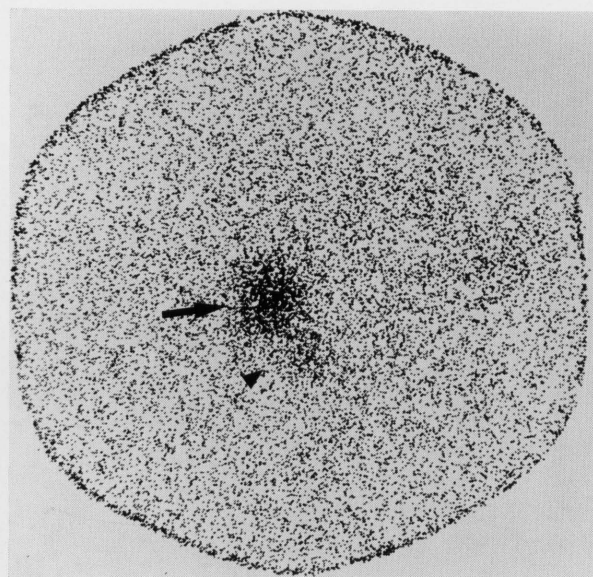
adenoma by histological examination of the removed specimen (Fig. 2). Concordant uptake was shown in all the 12 patients. The opposite adrenal was not entirely visualized in two patients with a hot nodule only. A left adrenal solid mass, 1.0 cm in diameter was visualized as a warm nodule in a 65-year-old
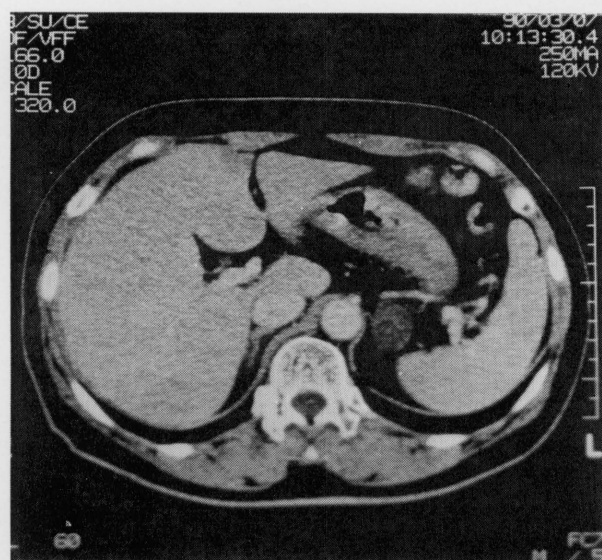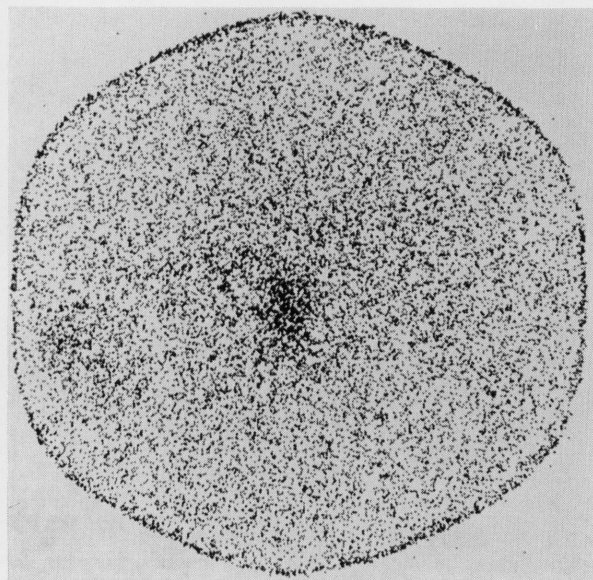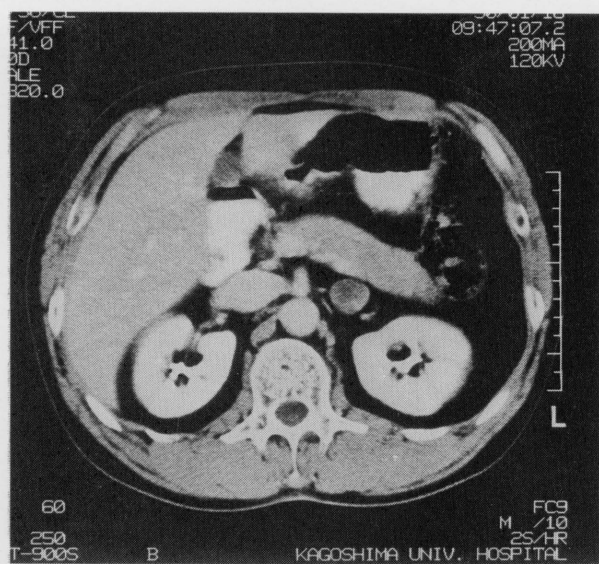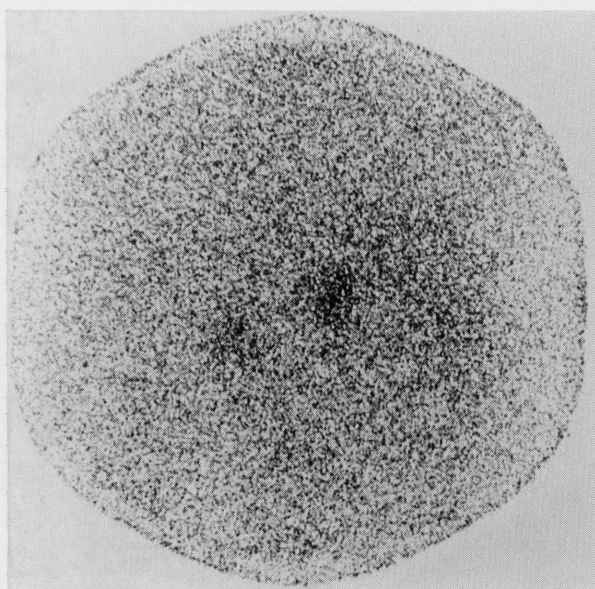
a

b

c

d

Fig. 2 A-58-year-old female patient with left adrenal silent adenoma. A left adrenal solid mass, 2.4 cm in diameter is shown in an abdominal CT scan (a). A concordant uptake is observed in the posterior adrenocortical scintigram obtained by using a multiparallel hole collimator (b). The mass is visualized as a hot nodule (*arrow*) which accompanies the adjacent adrenal tissue activity (*arrowhead*) in the left adrenal pinhole image (c). The right adrenal shows a normal pattern in the right adrenal pinhole image (d).

female patient with disconcordant uptake. A normal pattern was shown in the mass-bearing glands of 3 patients. Two of them were 55- and 63-year-old male patients, and had a 0.5 cm left and a 1.5 cm right adrenal solid mass, respectively. The remaining 69-year-old female patient had a 2.3 cm cyst located at the upper portion of the left adrenal. The concordant and symmetric uptakes were seen in one patient and two, respectively. A diffuse decrease was observed in the mass-bearing adrenals of 4 patients; a 67-year-old male with a 1.2 cm right adrenal solid mass, a 50-year-old male with a 7.5 cm right adrenal myelolipoma, a 60-year-old female with a 3.0 cm left adrenal ganglioneuroma and a 70-year-old fe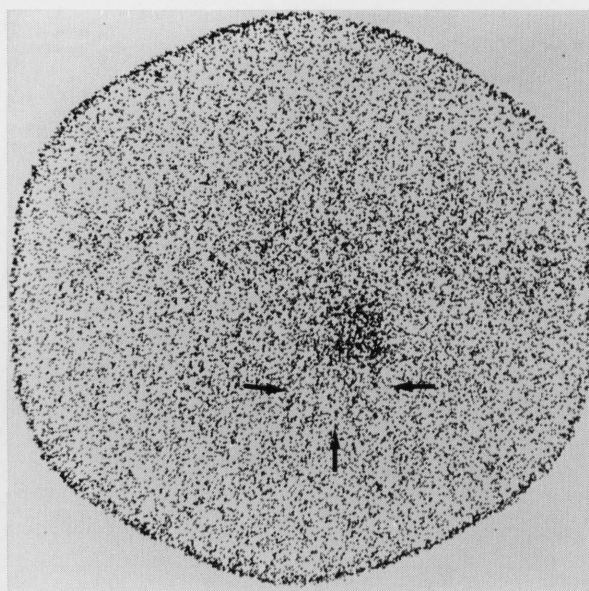male with a 0.9 cm left calcified adrenal. There were concordant uptake in one, symmetric uptake in one and disconcordant uptake in two. A partial defect was observed in the mass-bearing glands of 3 patients; a 46-year-old male with a 4.5 cm left adrenal cyst, a 24-year-old female with a 4.5 cm left adrenal cyst, and a 50-year-old female with a
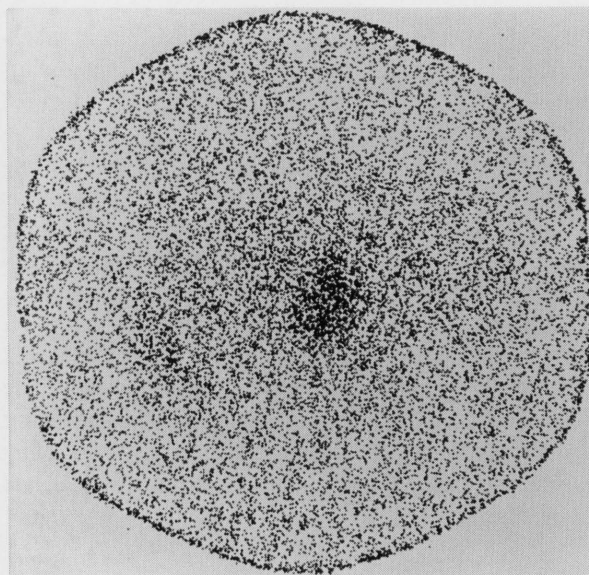
a

b

c

d

Fig. 3 A 54-year-old male patient with left adrenal metastasis from primary lung cancer (adenocarcinoma). A left adrenal solid mass, 2.0 cm in diameter is shown in an abdominal CT scan (a). A disconcordant uptake is observed in the posterior multiparallel hole adrenocortical scintigram (b). The left adrenal pinhole image (c) demonstrates a partial defect (c). The defect (*arrows*) is consistent with the mass located at the inferior portion of the adrenal in the CT scan. The right adrenal shows a normal pattern in the right adrenal pinhole image (d).

3.5 cm right adrenal pheochromocytoma. There were concordant uptake in one and disconcordant uptake in two. A complete defect was observed in the mass-bearing glands of 4 patients; a 57-year-old female with a 4.7 cm right adrenal solid mass, a 68-year-old male with a 8.3 cm right adrenal myelolipoma, a 34-year-old male with a 7.8 cm right adrenal ganglio-neuroma and a 60-year-old male with a 5.0 cm left adrenal pheochromocytoma. All patients with a complete defect had disconcordant uptake.

### 2. Malignant adrenal mass group.

This group consisted of 6 adrenal tumors. The diagnosis was confirmed by hormonal assays and pathological examinations of the removed or biopsied specimen in 3 patients with primary adrenocortical carcinoma, by assays of hormones and tumor-markers, serial CT examinations and clinical courses in 2 patients with primary lung carcinoma and by morphological examinations including CT, MRI and angiography and an avid uptake of a hepatobiliary imaging agent, ^{99m}Tc-PMT, in the tumor[19] in one patient with hepatocellular carcinoma, respectively. A large inhomogenous uptake was observed in a 8.0 cm right adrenal cortisol-producing carcinoma in a 51-year-old male. The opposite adrenal was not visualized in this patient. A partial defect was observed in the mass-bearing glands of two patients. The defects represented a 2.0 cm left adrenal metastasis in a 54-year-old male with primary lung adeno-carcinoma (Fig. 3) and a 2.3 cm right adrenal metastasis in a 66-year-old male with primary lung adenocarcinoma. These masses increased rapidly in size within 2 months. In the former there was disconcordant uptake, but in the latter symmetric uptake. A complete defect was observed in the mass-bearing glands of 3 patients. The masses were a 10.0 cm right adrenal nonfunctioning carcinoma in a 73-year-old male with disconcordant uptake, a 6.3 cm right adrenal metastasis in a 55-year-old male with hepatocellular carcinoma and disconcordant uptake, and a 9.8 cm left adrenal cortisol-producing carcinoma in a 58-year-old female with bilateral nonvisualization (Fig. 4).

3. Juxtaadrenal mass group.

This group consisted of 6 juxtaadrenal masses. The diagnosis was confirmed by pathological examinations of the removed specimen in all the patients. A normal pattern with normal location was observed in 4 patients; a 51-year-old female with a 2.8 cm left juxtaadrenal pheochromocytoma and disconcordant uptake, a 41-year-old female with a 1.5 cm left renal cell carcinoma located at the upper pole of the kidney and disconcordant uptake, a 60-year-old male with a 10.5 cm retroperitoneal carcinoma and
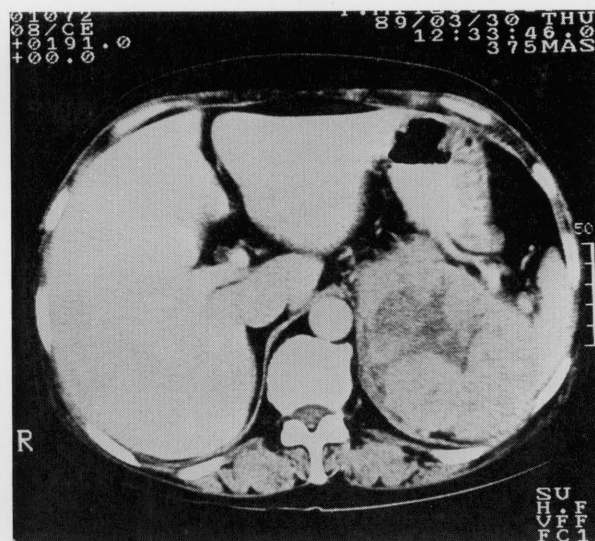
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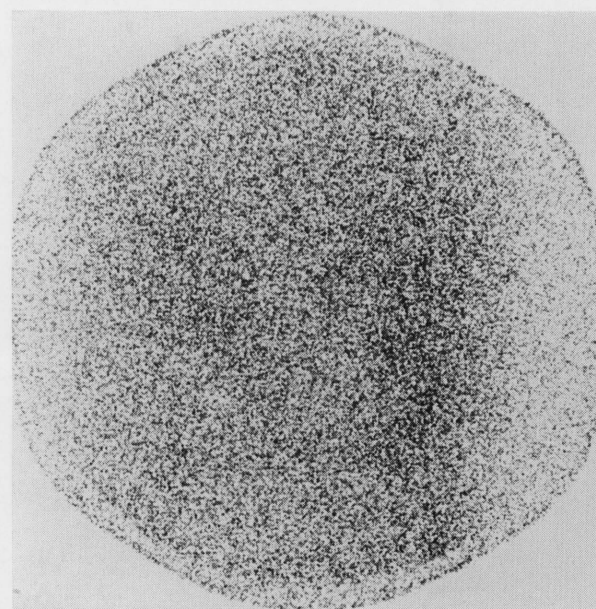
b

Fig. 4 A 58-year-old female patient with left adrenal cortisol-producing carcinoma. A 9.8 cm solid mass with irregular low density areas suggesting necrosis is shown in a CT scan (a). The posterior multiparallel hole adreno-cortical scintigram shows bilateral nonvisualization which is characteristic of cortisol-producing carcinoma.

symmetric uptake, and a 53-year-old female with a 3.3 cm degenerated neurilemmoma located at the left renal hilus and disconcordant uptake. The right concave adrenal deviated upward in a 54-year-old female with a 10.5 cm right renal hematoma and symmetric uptake. The left adrenal with a normal pattern deviated upward in a 40-year-old female with a 10.4 cm left-sided retroperitoneal teratoma and disconcordant uptake (Fig. 5).

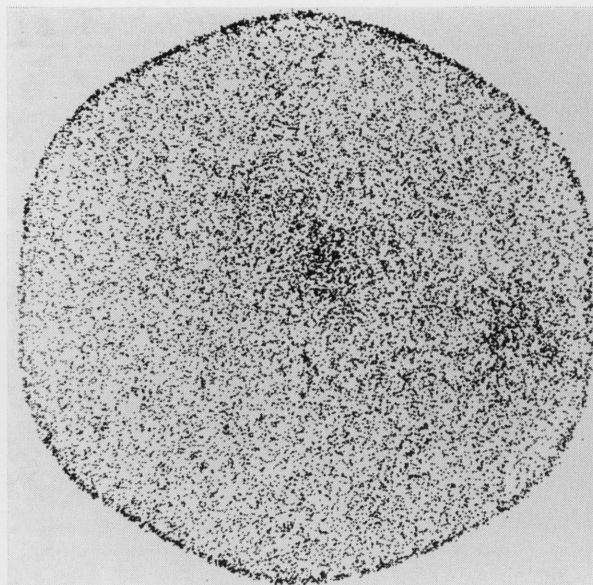Table 2 summarizes the relationships between the

imaging findings and the groups of benign, malignant adrenal and juxtaadrenal masses. Benign adrenal masses exhibited a wide range of imaging patterns from a hot nodule to a complete defect. In the malignant adrenal mass group, the imaging pattern was a partial or complete defect except one case of an
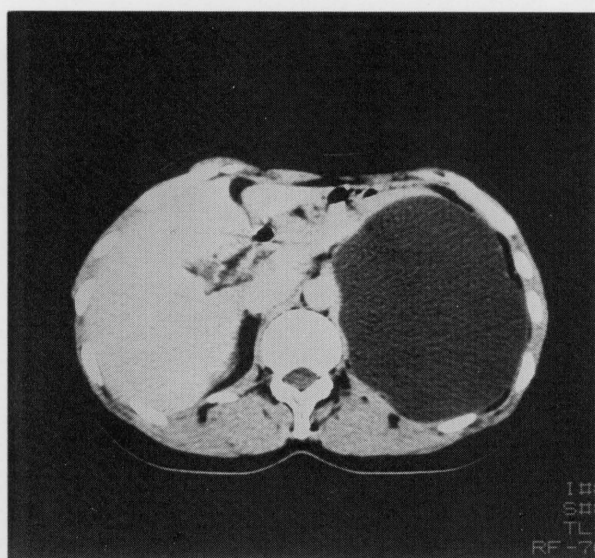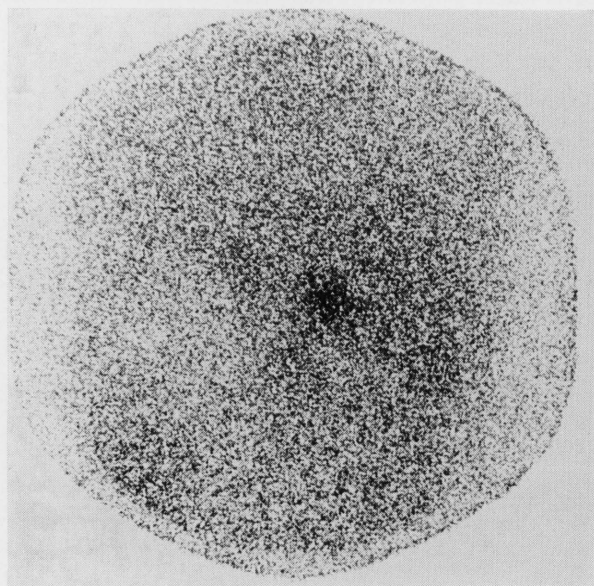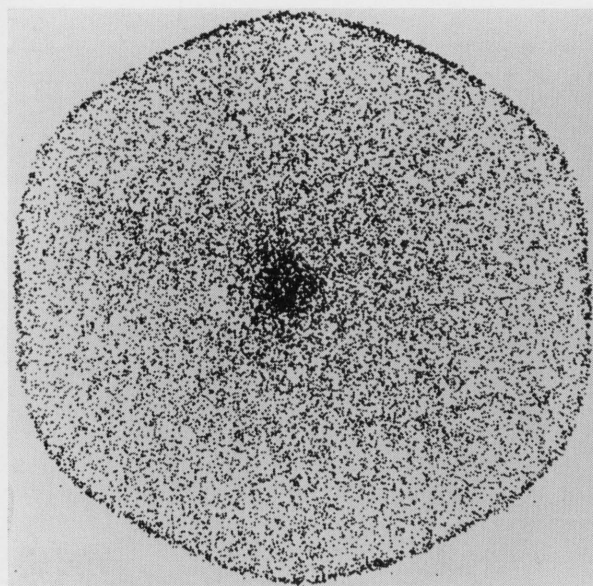

Fig. 5 A 40-year-old female patient with left juxta-adrenal retroperitoneal teratoma. A 10.5 cm low density mass is shown in a CT scan (a). The posterior multi-parallel hole adrenocrotical scintigram shows upper deviation of the left adrenal with disconcordant uptake (b). The appearances of the left (c) and right (d) adrenals are normal.

Table 2 Summary of the adrenocortical imaging findings of adrenal and juxtaadrenal masses

Group	N	Adrenocortical imaging findings*								
		H	HA	W	N	IU	DD	PD	CD	DV
BAM	27	2	10	1	3	0	4	3	4	0
MAM	6	0	0	0	0	1	0	2	3	0
JAM	6	0	0	0	4	0	0	0	0	2

* Abbreviations are the same as used in Fig. 1. BAM; benign adrenal mass group, MAM; malignant adrenal mass group, JAM; juxtaadrenal mass group.

inhomogenous uptake in a cortisol-producing carcinoma. A normal pattern or deviation with or without deformity was noted in the juxtaadrenal mass group.

4. Hyperfunctioning masses in the incidentally discovered adrenal and juxtaadrenal masses.

Of 33 adrenal and 6 juxtaadrenal masses, 4 adrenal-masses (2 pheochromocytomas and 2 cortisol-producing carcinomas) and one juxtaadrenal mass (pheochromocytoma) were judged to be hyperfunctioning when estimated by hormonal measurements of peripheral blood and urine. The imaging findings were a partial or complete defect in adrenal pheochromocytoma, a complete defect or inhomogeneous uptake without visualization of the opposite adrenal in cortisol-producing carcinoma and a normal pattern in juxtaadrenal pheochromocytoma.

5. Adrenal masses in oncologic patients.

There were 7 patients with pre- and post-operative known primary malignant extraadrenal neoplasms. Three patients had unilateral adrenal metastases (2 from lung cancer and one from hepatocellular carcinoma). The mass exhibited a partial defect in two and a complete defect in one. The remaining 4 patients were in a postoperative state of primary malignant neoplasms (each one: ureteral, rectal, urinary bladder and renal cell cancer). The adrenal masses in these patients were all benign. The mass exhibited a hot nodule in two, a normal pattern in one and a diffuse decrease in one, respectively.

DISCUSSION

The present study shows that adrenocortical scintigraphy can exhibit various types of image finding in incidentally discovered adrenal and juxtaadrenal masses. However, this variety is reasonable because of the characteristics of NCL-6-^{131}I and masses. Cholesterol is a principal precursor of steroid hormone biosynthesis. Therefore, NCL-6-^{131}I, a radio-labelled analog of cholesterol, is avidly taken up by the normal adrenal cortex, and also by hyperfunctioning and nonhyperfunctioning cortical adenomas.[13] A cortical carcinoma shows a complete or partial defect, inhomogenous or diffuse uptake, probably according to its differentiation and the presence or absence of necrosis and hemorrhage.[13,14] The uptake of this tracer in the adrenals is also related to the feedback mechanism between adrenocorticotropic hormone (ACTH) and glucocorticoid: An increase in serum ACTH stimulates adrenal uptake of the tracer, while a decrease suppresses the uptake.[13,20] Thus a decrease in serum ACTH due to autonomous serection of cortisol by an adrenal

tumor results in nonvisualization of ipsi- and contra-lateral adrenocortical tissues other than the tumor. An adrenal mass other than a cortical tumor may distort or destroy the adrenal cortex and result in a diffuse decrease, or a partial or complete defect according to its size and location in the adrenal.[13,14] A juxtaadrenal mass may produce a normal pattern in a normal location or deviation with or without deformity of the adrenal, depending on its size and location.[14,21]

In this series, an adrenal solid mass had a hot nodule with or without adjacent adrenal activity in 12 euadrenal patients. One of these masses was proved to be a cortical adenoma by histological examination. The remaining 11 masses should be silent or nonhyperfunctioning cortical adenomas.[15-17,22] Two patients with cortisol-producing carcinoma had a complete defect and an inhomogenous uptake with nonvisualization of the opposite adrenal, respectively. A diffuse decrease and a partial or complete defect were observed in benign noncortical massive lesions including 2 solid masses, 3 cysts, 2 myelolipomas, 2 ganglioneuromas, 2 pheochromocytomas and one calcified adrenal and 5 malignant tumors including 2 primary carcinomas and 3 metastases. Three benign solid masses had a normal pattern or a warm nodule probably due to their small size or nodular hyperplasia. A cyst located at the adrenal margin also had a normal pattern. A normal pattern was observed in 4 juxtaadrenal masses, and deviation of the adrenal was seen in 2 juxtaadrenal masses whose origins could not be preoperatively determind.

Diagnosis and management of incidentally discovered adrenal masses have been reviewed in several reports.[1,2,7,21,23-25] Determination of hormonal biochemical activity is a fundamental consideration.

In this series, 4 of 33 adrenal masses (12%) and one of 6 juxtaadrenal masses (17%) were hormonally hyperactive; 2 adrenal and one extraadrenal pheochromocytomas and 2 cortisol-producing cortical carcinomas. Two adrenal pheochromocytomas had nonspecific defect findings. If available, ^{131}I-meta-iodobenzylguanidine (MIBG) imaging should be performed in such pheochromocytoma patients because MIBG concentrates specifically in pheochromocytoma.[26,27] MRI also shows characteristic findings in this tumor.[4,6] Two patients with cortisol-producing carcinoma had a characteristic finding: a large inhomogenous uptake or complete defect of the tumor with nonvisualization of the opposite gland, suggesting autonomous secretion of cortisol by the tumor. The remaining 34 patients were euadrenal. Of the masses in these patients, 6 adrenal masses (3 cysts, 2 myelolipomas and one calcified adrenal) could be specifically diagnosed by CT or
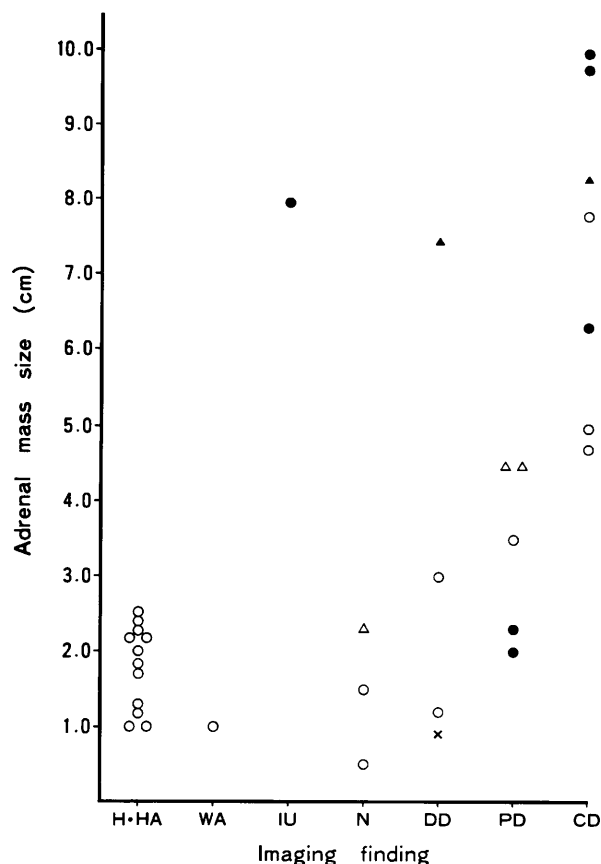
Fig. 6 The relationship between adrenocortical imaging and adrenal mass size. The abbreviations of imaging findings are shown in Fig. 1. ○; benign solid mass, ●; malignant solid mass, △; cyst, ▲; myelolipoma and ×; calcified adrenal.

US. Handling of the other solid masses involves problems. The size of the mass may be a reliable indicator of the nature of a biochemically silent lesion. Several authors differ as to the size of the mass, and this leads to different approaches to the incidentally discovered adrenal mass. Prinz et al[2] recommended that a mass greater than 3 cm in diameter should be surgically removed. Mitnich et al[5] suggest that a mass less than 5 cm in diameter with a smooth contour and well-defined margin may be followed up. Copeland[23] believes that those larger than 6 cm in diameter should be considered malignant unless proven otherwise. In our series, there were 27 adrenal solid tumors which could not be specifically diagnosed by CT or US (Fig. 6). If the 3 cm, 5 cm and 6 cm mass size criteria are applied to our series, a benign or malignant tumor is correctly diagnosed in 74% (20/27), 85% (23/27) and 89% (24/27), respectively. However such mass size criteria are invalid for adrenal masses in oncologic patients: Francis et al[15] reported 13 unilateral adenomas and 7 unilateral adrenal metastases 3 cm

or less in diameter in their series of 28 oncologic patients. Two of three adrenal metastases in our series were also less than 3 cm in diameter. It is clear that the nature of a mass cannot always be predicted on the basis of mass size alone, because the size of any mass is a function of time. Adrenocortical scintigraphy can predict the nature of a solid mass in the sense of cortical or noncortical origin. We could separate 12 silent adenomas and 2 cortisol-producing carcinomas from the other 13 solid masses by adrenocortical scintigraphy. Thus the scintigraphic approach can limit the number of patients sent for more invasive diagnostic procedures or operation. The imaging findings of juxtaadrenal masses were normal in 4 patients and upward deviation of the mass-side adrenal in each one with retroperitoneal teratoma and renal hematoma. One of us[14] previously reported scintigraphic findings in 4 such juxtaadrenal masses: Downward deviation of the left adrenal in 2 patients with splenic cysts and one with a left-sided retroperitoneal hematoma and upward deviation of the right adrenal in one patient with a right renal cyst. It is occasionally difficult to determine the origin of a retroperitoneal mass, especially in case of a large mass. Adrenocortical scintigraphy may be useful in differentiating a juxta-adrenal mass from an adrenal mass by showing a normal adrenal in its normal location or a deviated adrenal.

In conclusion, the role of adrenocortical scintigraphy in the evaluation of unilateral incidentally discovered adrenal or juxtaadrenal masses is to identify silent adenomas and cortisol-producing carcinomas among the adrenal masses and to help to discriminate juxtaadrenal from adrenal masses.

ACKNOWLEDGMENT

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