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Scintigraphy of incidentally discovered bilateral adrenal masses

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Abstract. The purpose of this study was to determine the patterns of iodine-131 6β-iodomethylnorcholesterol (NP-59) imaging and the correlation with computed tomography (CT)-guided adrenal biopsy and follow-up in patients with bilateral adrenal masses. To this end we investigated a consecutive sample of 29 euadrenal patients with bilateral adrenal masses discovered on CT for reasons other than suspected adrenal disease. Adrenal scintigraphy was performed using 1 mCi of NP-59 injected intravenously, with gamma camera imaging 5–7 days later. In 13 of the 29 patients bilateral adrenal masses were the result of metastatic involvement from lung carcinoma (5), lymphoma (3), adrenocarcinoma of the colon (3), squamous cell carcinoma of the larynx (1), and anaplastic carcinoma of unknown primary (1). Among these cases the NP-59 scan demonstrated either bilaterally absent tracer accumulation (in eight, all with bilateral metastases proven by CT-guided biopsy or progression on follow-up CT) or marked asymmetry of adrenocortical NP-59 uptake (in five). Biopsy of the adrenal demonstrating the least NP-59 uptake documented malignant involvement of that gland in five of five patients. In two patients an adenoma was found simultaneously in one adrenal with a contralateral malignant adrenal mass. In each of these cases, the adenoma demonstrated the greatest NP-59 uptake. In 16 patients diagnosis of adenoma was made on the basis of (a) CT-guided adrenal biopsy of the gland with the greatest NP-59 uptake of the pair (n=4), or (b) adrenalectomy (n=2), or (c) absence of change in the size of the adrenal mass on follow-up CT scanning performed 6 months to 3 years later (n=10). It is concluded that differential in vivo functional information provided by NP-59 scintigraphy complements that derived from anatomic imaging and can be used in patients with bilateral adrenal masses to select which gland would be the best choice for further diagnostic invasive evaluation (e.g., adrenal biopsy) or may suggest the presence of bilateral adrenal metastases in patients with incidentally discovered, bilateral adrenal masses.

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Introduction

The unexpected finding of a unilateral adrenal mass on computed tomography (CT) in a patient studied for reasons other than suspected adrenal dysfunction is not an uncommon occurrence in our sophisticated high-resolution, anatomical imaging environment [1–3]. The majority of these incidentally discovered masses or "incidentalomas" are benign, even in patients with known nonadrenal malignancies, despite the relatively high predilection for the adrenal as a site of metastasis of some tumors (e.g., lung and breast) [3–6]. Once their hormonal secretory status has been elucidated, further diagnostic attention must be paid to these masses to distinguish adrenal adenoma from metastasis [6–8].

In contrast, incidentally discovered bilateral adrenal masses are much less common. The diagnostic problems posed by bilateral adrenal masses have not been evaluated in large series, but have been noted anecdotally. In this report, we examine a subset of patients (29 of a total of 258) with incidentally discovered adrenal masses studied in our laboratory over a 16-year period. In previous reports we have documented the useful role of adrenocortical scintigraphy in depicting function of the unilateral, incidentally discovered, adrenal mass [4, 6, 9–11]. This report expands the use of iodine-131 6β-iodomethylnorcholesterol (NP-59) to the evaluation of patients with incidentally discovered, bilateral adrenal masses.

Table 1. NP-59 scintigraphy in bilateral nonhypersecretory adrenal masses

Imaging pattern	Lesion diameter (±SD)		Diagnosis
	Left (range)	Right (range)	
Bilateral symmetric visualization (8)	2.6±1.5 cm (2–5 cm)	2.2±1.5 cm (2–5 cm)	Adenoma (8)[a]
Bilateral asymmetric visualization (13)	2.4±1.4 cm (1–5 cm)	2.9±1.4 cm (1–5 cm)	Adenoma (8)[b] Carcinoma[c] Colon (2)[d] Lung (2)[d] Larynx (1)
Bilateral nonvisualization (8)	4.4±1.6 cm (2–7 cm)	5.6±1.7 cm (3.5–10 cm)	Carcinoma[e] Lung (3) Lymphoma (3) Colon (1) Anaplastic (1)

[a] Proven by no change in CT contour≥6 months in seven cases, and by CT-guided bilateral biopsy in one

[b] Proven by CT-guided adrenal biopsy in five cases (mass with increased NP-59 uptake) and by no change in CT contour in>6 months in three

[c] Proven by CT-guided adrenal biopsy (mass with decreased NP-59 uptake) in three cases and by bilateral biopsy in two

[d] One patient with an adrenal adenoma and a coexistent contralateral adrenal metastasis

[e] Proven by CT-guided adrenal biopsy of largest mass in three cases and by bilateral biopsy in four, and all with CT evidence of progression

Materials and methods

Between January 1976 and January 1992, 258 patients with adrenal masses discovered incidentally during CT examinations of the abdomen or chest performed for reasons other than clinically suspected adrenal disease were studied with NP-59 scintigraphy. Twenty-nine of the 258 patients had bilateral adrenal masses. CT was initially performed on an EMI-5005, and later on a Picker 1200SX at the VA Medical Center, Ann Arbor, and GE-8800 or GE-9800 scanners at the University of Michigan Medical Center. Contiguous 5- to 10-mm sections on the newer scanners were obtained after intravenous (IV) and/or oral radiographic contrast administration. Adrenal biopsies were performed either at or within 1 week of the time of the initial CT and were done before NP-59 scintigraphy.

All patients referred for NP-59 scintigraphy gave their written informed consent for the study, which was approved by each hospital's Institutional Review Board for Human Experimentation. One mCi of NP-59 was injected IV and was followed by posterior, anterior, and lateral abdominal scans (50000 counts per image) performed on days 5 and/or 7 after injection [12]. Saturated potassium iodide solution, 1 drop, was administered thrice daily, 24 h prior to and throughout the imaging sequence to suppress thyroidal uptake of free ^{131}I. A mild laxative (bisacodyl) was also given, 10 mg, twice daily, to most patients beginning 2 days before the 1st day of planned imaging to reduce potentially interfering colonic ^{131}I radioactivity [13].

In each patient various combinations of blood and urine biochemical measurements were obtained the exclude the presence of adrenal cortical or medullary dysfunction. These included in most cases, normal plasma levels of cortisol, renin activity, aldosterone, epinephrine, norephinephrine, urinary 17-hydroxycorticosteroids, 17-ketosteroids, and vanillymandelic acid, and normal cortisol responses to dexamethasone and in some cases adrenocorticotrophin (ACTH) administration. All medications that might interfere with either the scintigraphic or the biochemical studies were stopped prior to study. One of these 29 cases has been included in a study of scintigraphy in adrenal masses [9], and magnetic resonance imaging (MRI) of 10 of the 29 has been previously reported [14, 15].

The relationship of relative NP-59 uptake between the adrenals was assessed qualitatively. Under these circumstances evaluation was more difficult than with unilateral lesions as there was no morphologically normal adrenal in which the level of NP-59 uptake might be considered "normal" [10, 11]. Thus, in patients with CT-demonstrated bilateral adrenal masses, the presence of identifiable adrenal NP-59 uptake that visually approximated or exceeded that of the contralateral adrenal and/or liver (a tissue that accumulates NP-59) was considered compatible with a benign process (e.g., an adenoma), while markedly decreased or absent NP-59 uptake as compared to the contralateral adrenal and/or liver was considered abnormal and compatible with a destructive space-occupying or malignant adrenal mass. Bilaterally symmetric NP-59 uptake (within the limits of the normal and previously established degree of adrenal asymmetry) was considered normal [16]. Statistical analyses were performed using Student's *t* test [17].

Results

All 29 patients had bilateral adrenal masses on CT. The clinical indications for CT were a search for metastases in 17, abdominal pain in nine, and ascites, renal failure, and pneumonia in one case each. The mean lesion diameter was 3.3±1.4 cm (range: 1–7 cm) on the right, and

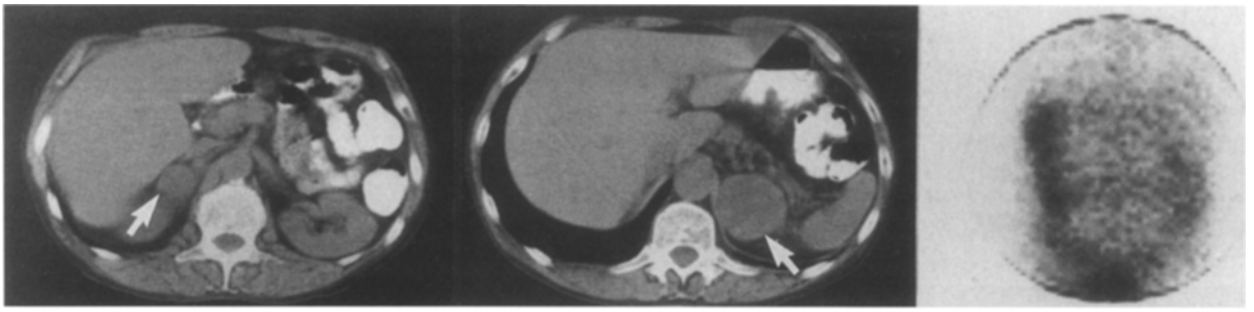

Fig. 1. CT scans (*left and center panels*) depict bilateral adrenal metastases (*arrows*) from lung carcinoma. Posterior NP-59 scan (*right panel*) shows bilateral non-visualization of the adrenals

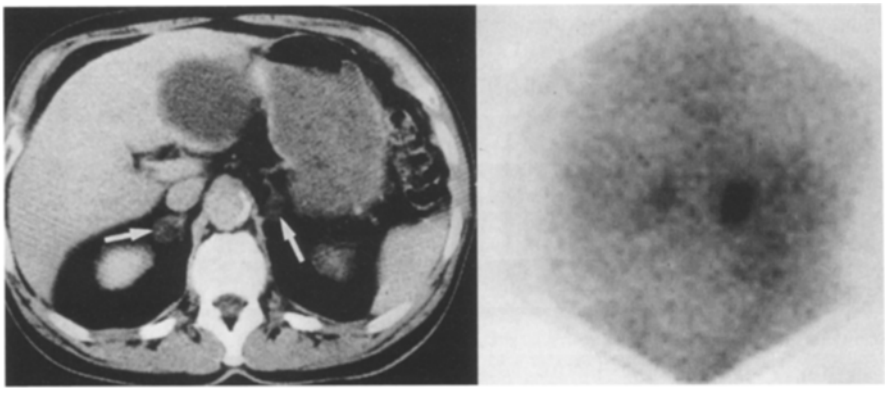

Fig. 2. CT scan (*left panel*) depicts bilateral adrenal masses (*arrows*) in a patient with metastatic adrenocarcinoma of the colon. Posterior NP-59 scan of the abdomen (*right panel*) demonstrates asymmetric tracer (right>left) uptake. CT-guided adrenal biopsy of the right adrenal was benign, while that of the left adrenal disclosed adenocarcinoma

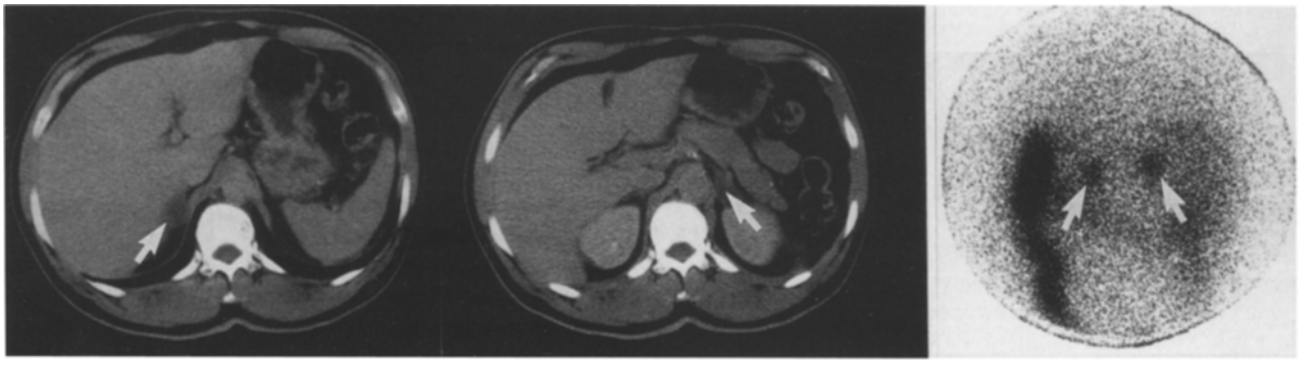

Fig. 3. CT scans (*left and center panels*) identify bilateral adrenal masses (*arrows*). Posterior abdominal NP-59 scan depicts symmetric adrenal uptake (*arrows*). Bilateral CT-guided adrenal biopsy was negative for malignancy

3.4±1.5 cm (range: 1–10 cm) on the left (P=ns) (Table 1). CT-guided adrenal biopsies were performed in 19 of the 29 patients. Unilateral adrenal biopsy was performed in 12 of 19 patients while bilateral adrenal biopsies were done in the remaining seven. Adrenal biopsy was performed as part of a research protocol during the interval from 1985 to 1988 [14, 15] while biopsies performed before 1985 and after 1988 were done as deemed necessary for clinical diagnostic purposes. All biopsies were done at the time of initial CT or shortly thereafter. Bilateral adrenal biopsies were performed when considered feasible, based upon the clinical status of the patient, accessibility of both masses for biopsy, and the degree of clinical suspicion of metastasis to the adrenals. When unilateral biopsies were performed, the larger of the two masses was usually selected for biopsy. Metastases were eventually determined to be present in 13 patients: lung carcinoma in five, lymphoma in three, adenocarcinoma of the colon in three, laryngeal carcinoma in one, and anaplastic carcinoma of unknown origin in one. In 16 cases an eventual diagnosis of adenoma was made by adrenal biopsy in four, by unilateral adrenalectomy in two, and by unchanged findings on repeat CT scans performed at 6 months to 3 years after the initial CT examination in the remaining 12 (including the two cases in which unilateral adrenalectomy was performed).

Variable patterns of NP-59 uptake were observed in the 29 patients with bilateral adrenal masses (Table 1). Bilateral nonvisualization was observed in eight patients in whom CT-guided adrenal biopsy confirmed metastatic involvement in one or both glands, and with progression on follow-up CT (Fig. 1). CT-guided adrenal biopsy performed in five of eight patients with asymmetric NP-59 uptake demonstrated that those adrenals with the greatest NP-59 accumulation of the pair (adrenal cortical uptake exceeding the contralateral adrenal or equal to liver) had benign cytology compatible with adenoma. The remaining three cases showed no change in adrenal contour over at least a 6-month follow-up period. Alternatively, CT-guided adrenal biopsy of masses exhibiting marked asymmetry of NP-59 uptake were the biopsy was directed to the gland exhibiting the least NP-59 uptake of the pair (less than the contralateral adrenal and/or liver) revealed metastatic disease on cytology in five of five patients (Table 1).

In two patients with markedly asymmetric NP-59 uptake, an adenoma in one adrenal was found to coexist with a contralateral metastatic deposit (lung and colon carcinoma, respectively) (Fig. 2), while of the remaining eight patients, all with bilaterally symmetric NP-59 uptake, seven had no change in adrenal contour over at least a 6-month follow-up period (Table 1). The remaining patient with bilateral 2-cm-diameter adrenal masses, had CT-guided biopsy evidence of adenoma (Fig. 3).

Discussion

Although a far less common problem, the clinical dilemma posed by incidentally discovered bilateral adrenal masses is not unlike that of the unilateral adrenal mass. Diagnosis is first dependent upon a hormonal evaluation sufficient to exclude either a hypersecretory state from bilateral adrenal sources or adrenal insufficiency due to complete destruction of the adrenal cortex [1, 2, 18]. Adrenal gland dysfunction with bilateral masses has been observed in primary aldosteronism [19], hypercortisolism due to either bilateral adenoma [20] or bilateral cortical nodular hyperplasia [21], congenital adrenal hyperplasia [22], pheochromocytoma particularly in the multiple endocrine neoplasia syndromes 2A and 2B [23, 24], and neuroblastoma [25]. Adrenocortical hypofunction with bilateral masses has been reported in tuberculosis [26], fungal diseases [27], bilateral adrenal hemorrhage [28], and rarely adrenal destruction from bilateral, primary adrenal neoplasms [29, 30] or as a result of bilateral metastases to the adrenals [31, 32]. The commonest sources of metastases to the adrenal are from lung carcinoma (bronchogenic) followed by breast, thyroid, and renal carcinoma, melanoma, and non-Hodgkin's lymphoma [31, 32]. In patients with underlying malignancy, adrenal metastases are usually noted in the presence of extensive metastatic disease to other sites (e.g., liver, bone, and lymph nodes). In this setting adrenal masses do not constitute a major diagnostic or therapeutic problem. However, when a patient has a known primary malignancy and adrenal masses and no other evidence of metastases, the presence of adrenal masses raises critical issues of tumor staging and further management.

Both CT and MRI have been used to identify bilateral adrenal masses and distinguish benign from malignant neoplastic involvement [2, 3, 15, 33–35]. Characteristic patterns of imaging seen on CT have demonstrated high sensitivity and specificity [33, 36, 37]. Recently developed MRI pulse sequences have been used to distinguish benign from malignant masses in some patients [38, 39]. However, up to one-third of adrenal masses may not be correctly characterized by CT or MRI [2, 14, 15, 40]. Many series of incidentally discovered adrenal lesions report a small number of patients who present on CT (or MRI) with incidentally discovered bilateral adrenal masses. These series have generally considered each of the neoplasms as separate lesions and interpretative attention has been placed upon an analysis of "individual" masses according to diagnostic criteria versus normal. There has not been a detailed comparison of one side versus the other with respect to anatomic and functional characteristics. Scintigraphic evaluations use the accumulation of radiocholesterol as an in vivo marker of differential adrenal cortical function. Thus, a reduction in or absence of adrenal ^{131}I-NP-59 uptake in non-dexamethasone-suppressed patients suggests adrenal gland replacement or destruction due to involvement with neoplasm or other space-occupying lesions [2, 4, 10, 11].

A nonexhaustive, but representative review of the literature published between 1981 and 1994 notes 632 cases of adrenal masses of which 108 (17%) were bilateral [5–8, 14, 33, 35, 37, 39–49] (Table 2). Of those patients with bilateral adrenal masses in whom data were available that distinguished benign from malignant masses, 52% had malignant involvement of the adrenals. In the present series, 29 of 258 (11%) had incidentally discovered bilateral adrenal masses, and 13 of the 29 (45%) had metastatic disease to one (2 of 13) or both (11 of 13) adrenals. Bilateral benign masses were noted in 16 of the 29 patients (55%) despite the fact that 17 (59%) had a preexisting malignancy. Thus, in our series it is slightly more likely that a patient presenting with bilateral adrenal masses would have bilateral benign rather than malignant adrenal involvement, even in the presence of a preexisting malignancy elsewhere. Our data may differ from the published literature as a result of referral bias, as we considered only those cases of truly incidental and nonhypersecretory adrenal masses.

More intriguing is the simultaneous presence of a benign non-hypersecreting adenoma and a contralateral adrenal metastasis, a phenomenon that has been previously reported [41, 45] and was documented in two cases in our series. Furthermore, multiple metastases to one gland [45] and an unusual case of a metastasis to an adrenal adenoma have also been noted [50]. There are also reports of bilateral adrenal masses in which one adrenal lesion was hypersecreting (e.g., aldosteronoma) while the

Table 2. Bilateral adrenal masses

Authors	Year	Total cases	Bilateral	Benign	Malignant
Cedarmark and Ohlsen	1981	5[a]	2	0	2[d]
Zornoza et al.	1981	21[a]	2[b]	–	–
Heaston et al.	1982	14[c]	2	1	1
Berkman et al.	1984	16	2[b]	–	–
Oliver et al.	1984	32	6	4	2
Hussain et al.	1985	43[a]	5	2	3
Abecasis et al.	1985	21	2	2	0
Katz and Shirkhoda	1985	16[c]	7	3	4
Belldegrun et al.	1986	38[a]	6	3	3[d]
Hussain et al.	1986	57	6	0	6
Glazer et al.	1986	28[a]	5	2	3
Doppman et al.	1987	81[a]	13[b]	–	–
Berland et al.	1988	44[e]	7[b,f]	–	–
Reincke et al.	1989	32[a]	8[b]	–	–
Krestin et al.	1989	25[a]	4	2	2
Virkkala et al.	1989	20	2	2[g]	0
Khafagi et al.	1991	45[h]	6	0	6
Jockenhovel et al.	1992	36[a]	4[b]	–	–
Reinig et al.	1994	53[a]	7[b]	–	–
Haab et al.	1994	12[a]	12	10	2
Total		632	108 (17%)	31 (48%)	34 (52%)

[a] Series with hypersecreting and nonhypersecreting adrenal masses
[b] Did not distinguish bilateral benign from bilateral malignant masses
[c] Patients with known preexisting malignancy
[d] Patient with coexisting ipsilateral benign and contralateral adrenal metastasis
[e] Masses all <5 cm in diameter
[f] Either bilateral benign or bilateral malignant masses
[g] Patient with nonsuppressible urinary cortisol metabolites
[h] Masses all ≥5 cm in diameter

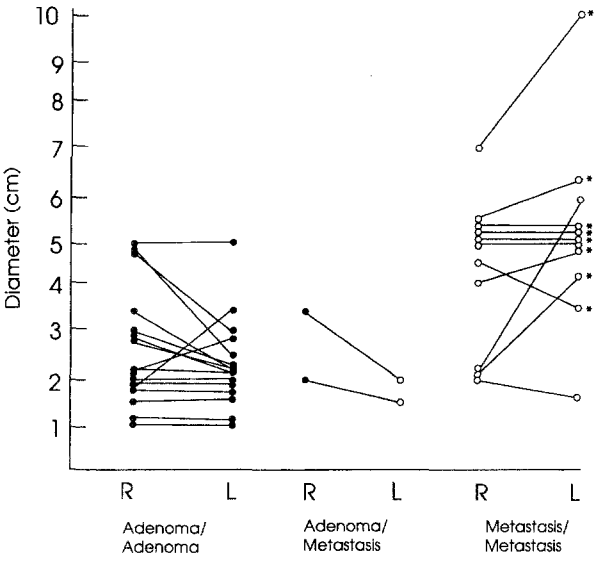

Fig. 4. Diameter of adrenal bilateral masses. Each connected pair denotes the adrenal masses in a single patient. *R*, Right adrenal; *L*, left adrenal; ●, adenoma; ○, metastasis; *, nonvisualization on NP-59 scintigraphy

other was a nonhypersecreting adenoma [51, 52]. Perhaps, a slowly expanding intra-adrenal metastasis, a less aggressive primary malignancy, or a nonglucocorticoid hypersecreting neoplasm would allow the development of compensatory hyperplasia leading to a functioning, but not hypersecretory, contralateral adrenal mass [53].

Recommendations for further diagnostic evaluations based upon the size of an adrenal mass alone may be misleading. Thus, in a patient with bilateral masses and a preexisting cancer, biopsy of the larger of the two masses may not invariably disclose the presence of malignancy. In the current series, 2 of 29 patients (2 of 13 with asymmetric NP-59 uptake) had an adenoma and a contralateral metastasis where the malignant mass was smaller (2 and 3 cm versus 3 and 4 cm, respectively) than the benign adenoma. As a group the sizes of the malignant masses were not significantly greater than the sizes of those that were benign (Fig. 4). Further, in two reports of patients with primay aldosteronism and bilateral adrenal masses the smaller of the two masses was later proven to be an aldosterone-secreting adenoma while the larger mass was a nonhypersecretory adenoma [51, 52].

The scintigraphic evaluation of bilateral incidentally

discovered adrenal masses represents a far more difficult problem than for unilateral lesions as the present interpretative algorithm depends upon the presence of an anatomically normal contralateral adrenal gland (by CT criteria) for comparison [10]. Accumulation of NP-59 that approaches or exceeds that of liver, a tissue that accumulates NP-59, and bilateral but asymmetric NP-59 uptake (that exceeds normal adrenal asymmetry) may be useful in guiding further invasive evaluation. In six cases (including the adenomas in the two patients with coexistent contralateral malignant masses) biopsy and in two cases adrenalectomy of the most prominent adrenal (that gland with the most NP-59 uptake as assessed visually) were benign, while biopsy of the adrenal mass with the least NP-59 uptake of the pair disclosed adrenal metastases in five cases. While these numbers are small, the results of NP-59 imaging in bilateral adrenal masses suggests that further studies (e.g., adrenal biopsy) would be best directed toward the adrenal mass with the least iodocholesterol uptake, since in a patient with a known malignancy it usually matters little to further diagnostic evaluation and therapy whether one or both glands are affected. Bilateral masses on CT with bilateral nonvisualization of the adrenals on NP-59 scintigraphy was predictive of bilateral metastases in eight of eight patients. It was perhaps not surprising that this group had the largest adrenal masses (Table 1). The scintiscan depicts adrenal cortical effacement by neoplasm, a pattern of imaging that has been previously described [2, 6, 10, 11, 54]. In some cases, exogenous hormone therapy to protect against the development of adrenocortical insufficiency may be contemplated if both adrenals are replaced by a metastatic or other infiltrative processes [28–31]. It is, however, unusual for patients to present with adrenal cortical insufficiency from bilateral adrenal metastases since more than 90% of the adrenal must be replaced before cortical hypofunction becomes clinically apparent [30, 31].

Scintigraphy of bilateral adrenal masses may provide unique, non-invasive information regarding relative differential adrenal function that can be used to identify lesions requiring further diagnostic evaluation [5]. The data available to date document that adrenal masses, and especially bilateral adrenal masses, are of heterogeneous etiology. With respect to our series of incidentally discovered bilateral adrenal masses, the following conclusions seem most appropriate:

1. Bilateral masses in patients with malignancies appear to be slightly more likely to be adenomas than metastases.
2. Although the larger the mass the greater the likelihood of malignancy, size remains a poor discriminator of malignancy in patients with bilateral adrenal masses in the 2–5 cm range.
3. Although the situation is uncommon, an adrenal adenoma and a contralateral adrenal malignancy can coexist.
4. NP-59 may be used to functionally characterize bilateral (and unilateral) adrenal neoplasms and as a means to select masses for further diagnostic evaluation(s).

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References

1. Copeland PM. The incidentally discovered adrenal mass. *Ann Intern Med* 1983; 98:940–945.
2. Francis IR, Gross MD, Shapiro B, Korobkin M, Quint LE. Integrated imaging of adrenal disease. *Radiology* 1992; 184:1–13.
3. Gajraj H, Young AE. Adrenal incidenaloma. *Br J Surg* 1992; 80:422–426.
4. Francis IR, Smid A, Gross MD, Shapiro B, Naylor B, Glazer G. Adrenal masses in oncologic patients: functional and morphologic evaluation. *Radiology* 1988; 166:353–356.
5. Oliver TW, Bernardino ME, Miller JI, Mansour K, Greene D, Davis WA. Isolated adrenal masses in non-small cell bronchogenic carcinoma. *Radiology* 1984; 153:217–218.
6. Khafagi F, Gross MD, Shapiro B, Glazer GM, Francis I, Thompson NW. Clinical significance of the large adrenal mass. *Br J Surg* 1991; 78:828–833.
7. Katz RL, Shirkhoda A. Diagnostic approach to incidental adrenal nodules in the cancer patient: results of a clinical, radiologic, and fine-needle aspiration study. *Cancer* 1985; 55:1995–2000.
8. Berkman WA, Bernardino ME, Sewell CW, Price RB, Sones PJ Jr. The computed tomography-guided adrenal biopsy: an alternative to surgery in adrenal mass diagnosis. *Cancer* 1984; 53:2098–2103.
9. Gross MD, Wilton G, Shapiro B, Cho K, Samuels BI, Bouffard AJ. Functional and scintigraphic evaluation of the silent adrenal mass. *J Nucl Med* 1987; 28:1401–1407.
10. Gross MD, Shapiro B, Bouffard AJ, et al. Distinguishing benign from malignant euadrenal mass. *Ann Intern Med* 1988; 109:613–618.
11. Gross MD, Shapiro B, Francis IR, et al. Scintigraphic evaluation of the clinically silent adrenal mass. *J Nucl Med* 1994; 35:445–452.
12. Gross MD, Valk TW, Swanson DP, Thrall JH, Grekin RJ, Beierwaltes WH. The role of pharmacologic manipulation in adrenal cortical scintigraphy. *Semin Nucl Med* 1981; 9:128–156.
13. Shapiro B, Nakajo M, Gross MD, Freitas JE, Copp JE, Beierwaltes WH. Value of bowel preparation in adrenocortical scintigraphy with NP-59. *J Nucl Med* 1983; 24:732–734.
14. Glazer GM, Woolsey EJ, Borrello J, et al. Adrenal tissue characterization using MR imaging. *Radiology* 1986; 158:73–79.
15. Remer EM, Weinfield RM, Glazer GM, et al. MRI characterization and comparison of hyperfunctioning and nonhyperfunctioning benign adrenal cortical lesions. *Radiology* 1989; 171:681–685.
16. Freitas JE, Thrall JH, Swanson DP, Rifai A, Beierwaltes WH. Normal adrenal asymmetry: explanation and interpretation. *J Nucl Med* 1978; 19:149–154.

17. Remington RD, Schork MA. Statistics with applications to biological health sciences. Englewood Cliffs, N.J.: Prentice-Hall; 1970:19:149–154.
18. Ross NA, Aron DC. Hormonal examination of the patient with an incidentally discovered adrenal mass. *N Engl J Med* 1990; 323:1401–1405.
19. Ferriss JB, Beevers DG, Brown JJ, et al. Clinical, biochemical and pathological fetures of low-renin ('primary') hyperaldosteronism. *Am Heart J* 1978; 95:375–388.
20. Mimou N, Sakato S, Nakabayashi H, Saito Z, Takeda R, Matsubara F. Cushing's syndrome associated with bilateral adrenal adenomas. *Acta Endocrinol* 1985; 108:245–254.
21. Fig LM, Gross MD, Shapiro B, et al. Adrenal localization in the adrenocorticotrophic hormone-independent Cushing's syndrome. *Ann Intern Med* 1988; 109:547–553.
22. Falke THM, te Strake LE, Shaff MI, et al. Magnetic resonance imaging of the adrenal glands. *J Comput Assist Tomogr* 1986; 10:242–253.
23. Cryer PE. Pheochromocytoma. *Clin Endocrinol* 1985; 14:203–220.
24. Webb TA, Sheps SG, Carney JA. Differences between sporadic pheochromocytoma and pheochromocytoma in multiple endocrine neoplasia type 2. *Am J Surg Pathol* 1980; 4:121–126.
25. Gonzalez-Crussi F, Hsueh W. Bilateral adrenal ganglioneuroblastoma with neuromelanin. Clinical and pathologic observations. *Cancer* 1988; 61:1159–1166.
26. McMurray JF, Long D, McClure R, Kotchen TA. Addison's disease with adrenal enlargement on computed tomographic scanning. *Am J Med* 1984; 77:365–368.
27. Wilson DA, Muchmore HG, Tisdal RG, Fahmy A, Pitha JV. Histoplasmosis of the adrenal glands studied by CT. *Radiology* 1984; 150:779–783.
28. Dahlberg PJ, Goellner MH, Pehling GH. Adrenal insufficiency secondary to adrenal hemorrhage. Two case reports and a review of cases confirmed by computed tomography. *Arch Intern Med* 1990; 150:905–909.
29. Paling MR, Williamson BRJ. Adrenal involvement in non-Hodgkin lymphoma. *Am J Roentgenol* 1983; 141:303–305.
30. Kung AW, Pun KK, Lam K, Wang C, Leung CY. Addisonian crisis as presenting feature in malignancies. *Cancer* 1990; 65:177–179.
31. Seidenwurm DJ, Elmer EB, Kaplan LM, Williams EK, Morris DG, Hoffman AR. Metastases to the adrenal gland and the development of Addison's disease. *Cancer* 1984; 54:552–557.
32. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma. Analysis of 1000 autopsied cases. *Cancer* 1950; 3:78–85.
33. Hussain S, Belldegrun A, Seltzer SE, Richie JP, Abrams HL. CT diagnosis of adrenal abnormalities in patients with primary non-adrenal malignancies. *Eur J Radiol* 1986; 6:127–131.
34. Dunnick NR. Adrenal imaging: current status. *Am J Roentgenol* 1990; 154:927–936.
35. Doppman JL, Rening JW, Dewyer AJ, Frank JP, Norton J, Loriaux DL, Keiser H. Differentiation of adrenal masses by magnetic resonance imaging. *Surgery* 1987; 102:1018–1026.
36. Berland LL, Koslin DB, Kenney PH, Stanley RJ, Lee JY. Differentiation between small benign and malignant adrenal masses with dynamic incremented CT. *Am J Roentgenol* 1988; 151:95–101.
37. Hussain S, Belldegrun A, Seltzer SE, Richie JP, Gittes RF, Abrams HL. Differentiation of malignant from benign adrenal masses: predictive indices on computed tomography. *Am J Roentgenol* 1985; 144:61–65.
38. Mitchell DG, Corvello M, Matteucci T, Petersen RO, Miettinen MM. Benign adrenocortical masses: diagnosis with chemical shift MR imaging. *Radiology* 1992; 185:345–351.
39. Krestin GP, Steinbrich W, Friedmann G. Adrenal masses: evaluation with fast gradient-echo MR imaging and Gd-DTPA-enhanced dynamic studies. *Radiology* 1989; 171:675–680.
40. Reinig JW, Stutley JE, Leonhardt CM, Spicer KM, Margolis M, Caldwell CB. Differentiation of adrenal masses with MR imaging: comparison of techniques. *Radiology* 1994; 192:41–46.
41. Cedermark BJ, Ohlsen H. Computed tomography in the diagnosis of metastases of the adrenal gland. *Surg Gynecol Obstet* 1981; 152:13–16.
42. Zornoza J, Ordonez N, Bernardino ME, Cohen MD. Percutaneous biopsy of adrenal tumors. *Urology* 1981; 18:412–416.
43. Heaston DK, Handel DB, Ashton PR, Korobkin M. Narrow gauge needle aspiration of solid adrenal masses. *Am J Roentgenol* 1982; 138:1143–1148.
44. Abecasis M, McLoughlin M, Langer B, Kudlow JE. Serendipitous adrenal masses: prevalence, significance, and management. *Am J Surg* 1985; 149:783–788.
45. Belldegrun A, Hussain S, Seltzer SE, Loughlin KR, Gittes RF, Richie JP. Incidentally discovered mass of the adrenal gland. *Surg Gynecol Obstet* 1986; 163:203–208.
46. Reincke M, Winkelman W, Jaursch-Hancke C, Kaulen D, Nike J, Ollenschlager G, Allolio B. Diagnostik and Therapie asymptomatischer Nebennierentumoren. *Dtsch Med Wochenschr* 1989; 114:861–865.
47. Virkkala A, Valimaki M, Pelkonen R, et al. Endocrine abnormalities in patients with adrenal tumors incidentally discovered on computed tomography. *Acta Endocrinol (Copenh)* 1989; 121:67–72.
48. Jockenhovel F, Kuck W, Hauffa B, et al. Conservative and surgical management of incidentally discovered adrenal tumors (incidentalomas). *J Endocrinol Invest* 1992; 15:331–337.
49. Haab F, Duclos JM, Julien J, Plovin PF. Tumeurs des deux surrenales. 12 Cas Consecuties. *Presse Med* 1994; 23:511–514.
50. Mizuo H. Scintigraphic demonstration of lung cancer metastases to adrenal adenoma; a pitfall in adrenal scintigraphy. *Jpn J Clin Radiol* 1993; 38:633–635.
51. Herd GW, Semple PF, Parker D, Davidson JK, Hilditch TE, Fraser R. False localization of an aldosteronoma by dexamethasone-suppressed adrenal scintigraphy. *Clin Endocrinol* 1987; 26:699–705.
52. Shapiro B, Grekin RJ, Gross MD, Freitas JE. Interference of spironolactone on adrenocortical scintigraphy and other pitfalls in the location of adrenal abnormalities in primary aldosteronism. *Clin Nucl Med* 1994; 19:441–445.
53. Gross MD, Shapiro B, Freitas JE, et al. Clinical significance of the solitary functioning adrenal gland. *J Nucl Med* 1991; 32:1882–1887.
54. Quraishi MA, Costanzi JJ, Balachandran S. Iodocholesterol adrenal scanning for the detection of adrenal metastases in lung cancer and its clinical significance. *Cancer* 1981; 48:714–716.