

Evaluation and surgical resection of adrenal masses in patients with a history of extra-adrenal malignancy

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Background. Adrenal abnormalities are often identified on imaging studies performed during the staging of patients presenting with a new malignancy or restaging of patients with a history of a malignancy.

Methods. We reviewed the records of patients who underwent surgical resection of an adrenal mass identified in the setting of previously or newly diagnosed extra-adrenal malignancy.

Results. Eighty-one patients with an adrenal mass and recently diagnosed malignancy ($n = 24$) or history of a malignancy ($n = 57$) underwent adrenalectomy. In 42 patients (52%) the adrenal mass was a metastasis. In 39 patients (48%) the adrenal mass was an additional primary adrenal tumor process: 19 pheochromocytomas, (14 syndrome-associated, 5 sporadic), 13 cortical adenomas, 3 adrenocortical carcinomas, 2 ganglioneuromas, and 2 cases of nodular hyperplasia.

Conclusions. In this series nearly half of the patients with cancer and an adrenal mass had adrenal pathologic condition independent of their primary malignancy. Despite the presence of a newly diagnosed malignancy or history of malignancy, all patients with an adrenal mass should undergo a standard hormone evaluation to confirm that the mass is not a functional neoplasm. An assumption that the adrenal mass is metastatic disease will be wrong in up to 50% of such patients. (Surgery 2001;130:1060-7.)

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ADRENAL MASSES ARE IDENTIFIED in up to 4% of patients undergoing computed tomography (CT) scanning of the abdomen or chest.¹ Because metastases involving the adrenal gland are frequently seen as a component of the natural history of a number of relatively common malignancies, including renal cell carcinoma, malignant melanoma, and carcinoma of the lung, colon, and rectum,²⁻⁵ adrenal masses identified during the radiographic staging of a newly diagnosed malignancy or radiographic surveillance after therapy for a previously treated malignancy are often assumed to be metastatic lesions.⁶⁻⁸ However, the

assumption that an adrenal mass identified in a patient with a concurrent or prior extra-adrenal cancer is a metastasis rather than an independent tumor process may result in unnecessary and inappropriate cancer-directed therapy. In addition, failure to recognize that an adrenal mass identified in a cancer patient may represent a process independent of the index malignancy may result in delayed or incorrect treatment of a primary adrenal pathologic condition. To determine more accurately which patients with relatively limited extra-adrenal cancer are more likely to have metastatic disease versus a primary adrenal mass unrelated to the index cancer, we retrospectively reviewed all patients who underwent resection of an adrenal mass in the setting of a prior or concurrent extra-adrenal malignancy in a tertiary referral cancer center.

PATIENTS AND METHODS

The medical records of 196 patients with tumors involving the adrenal gland who were referred for evaluation and underwent adrenalectomy

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Table I. Extra-adrenal cancer diagnoses in 81 patients presenting with an adrenal mass*

<i>Cancer diagnosis</i>	<i>No. of patients</i>	<i>Prior diagnosis of extra-adrenal cancer</i>	<i>Synchronous diagnosis of extra-adrenal cancer</i>	<i>Unilateral adrenal mass</i>	<i>Bilateral adrenal masses</i>
Renal cell carcinoma	27	18	9	24	3
Melanoma	13	10	3	12	1
Medullary thyroid cancer	11	10	1	6	5
Colorectal cancer	7	5	2	7	0
Prostate cancer	6	6	0	5	1
Non-small cell lung cancer	5	4	1	5	0
Breast cancer	2	2	0	2	0
Cervical cancer	2	2	0	2	0
Gastrointestinal stromal tumor	2	2	0	2	0
Basal cell carcinoma	2	2	0	2	0
Pancreatic adenocarcinoma	1	0	1	1	0
Pancreatic neuroendocrine tumor	1	0	1	1	0
Duodenal adenocarcinoma	1	1	0	1	0
Cholangiocarcinoma	1	0	1	1	0
Rectal carcinoid	1	0	1	1	0
Transitional cell carcinoma, renal pelvis	1	0	1	1	0
Transitional cell carcinoma, bladder	1	1	0	1	0
Squamous cell carcinoma, lip	1	1	0	1	0
Squamous cell carcinoma, sacrum	1	0	1	1	0
Choriocarcinoma	1	1	0	0	1
Seminoma	1	1	0	0	1
Thymoma	1	0	1	1	0
Chronic myelogenous leukemia	1	1	0	1	0
Unknown primary cancer	1	0	1	1	0
Total (%)	91	67 (74)	24 (26)	79 (87)	12 (13)

*Ten patients had 2 separate extra-adrenal cancer diagnoses.

tomy at The University of Texas M. D. Anderson Cancer Center from 1971 to 2000 were reviewed. Of these patients, 115 had no history of extra-adrenal malignancy; none of these patients had metastasis to the adrenal gland from an unknown primary cancer, confirming the rare nature of this presentation.⁷ Eighty-one of the 196 patients had 1 or more previously or synchronously diagnosed extra-adrenal malignancies. The medical records of these 81 patients were retrospectively reviewed to determine the results of laboratory testing, radiographic evaluation, histopathologic diagnosis, and surgery as well as to obtain follow-up and survival information. Because of the retrospective nature of the study representing more than 29 years of clinical experience, extent of evaluation (eg, preoperative hormone screening) and treatment (eg, open vs laparoscopic adrenalectomy) were not necessarily standardized. Estimates of adrenal tumor size were obtained from the surgical pathology report; adrenal tumor size was recorded as the greatest cross-sectional dimension reported. When the pathology report did not specify a tumor size (29 patients), the size of the adrenal tumor was

recorded as the greatest cross-sectional diameter reported on radiographic imaging studies (CT or magnetic resonance imaging [MRI]). Follow-up was current through February 2001. Patient survival duration was measured from the date of adrenalectomy. The survival distribution was estimated with the product-limit method described by Kaplan and Meier, and the survival data of the subgroups were compared with log-rank analysis. Calculations were performed with STATISTICA 5.5 for Windows (StatSoft, Tulsa, Okla).

RESULTS

There were 81 patients with an adrenal mass in the setting of a prior or concurrent diagnosis of 1 or more extra-adrenal malignancies who were treated by adrenalectomy. Ten of the patients had 2 extra-adrenal malignancies, resulting in a total of 91 cancer diagnoses (Table I). In 57 patients (70%) the adrenal mass was identified in the setting of a prior diagnosis of malignancy, and in 24 patients (30%) the adrenal mass was identified during evaluation for a newly identified malignancy. Seventy-one patients (88%) had a unilateral adrenal mass,

Table II. Clinical characteristics of 42 patients with metastasis to the adrenal gland

<i>Cancer diagnosis</i>	<i>No. of patients</i>	<i>No. of patients with bilateral adrenal metastases</i>	<i>No. of patients with metastases limited to the adrenal gland*</i>	<i>No. of patients with synchronous extra-adrenal metastasis*</i>
Renal cell carcinoma	24	1	20	4
Melanoma	7	1	6	1
Colorectal cancer	4	0	3	1
Prostate cancer	3	1	3	0
Non-small cell lung cancer	2	0	2	0
Choriocarcinoma	1	1	1	0
Unknown primary cancer	1	0	1	0
Total (%)	42	4 (10)	36 (86)	6 (14)

*At the time of surgical resection.

and 10 (12%) had bilateral adrenal masses. Eighty-four adrenalectomies were performed via open laparotomy; 7 were performed via laparoscopy. Six patients with bilateral tumors underwent a cortical-sparing partial adrenalectomy (5 pheochromocytomas, 1 melanoma).⁹ The median size of the resected adrenal lesions was 3.5 cm (mean, 4.3 cm; range, 0.8 to 20.0 cm).

In 42 patients (52%) the adrenal mass was a metastasis from an extra-adrenal malignancy (Table II). The median size of the resected adrenal metastases was 3.8 cm (mean, 4.2 cm; range, 0.0 to 19.5 cm). In these patients the most common source of metastasis to the adrenal gland was renal cell carcinoma (24 patients, 57%) followed by melanoma, colorectal cancer (colon, 3 patients; rectal, 1 patient), prostate cancer, and non-small cell lung cancer. Bilateral metastases to the adrenal gland were seen in 4 patients (10%). Fifteen patients (36%) had extra-adrenal distant metastatic disease identified either concurrently with or before their adrenal metastasis. In contrast, in 27 patients (64%) distant metastatic disease was clinically and radiographically limited to the adrenal gland. In 36 patients (86%) distant metastatic disease was limited to the adrenal gland at the time of resection, whereas in another 3 patients (7%) limited extra-adrenal distant metastatic disease amenable to complete surgical resection at the time of adrenalectomy was present. Finally, in 3 patients complete resection of metastatic disease was not feasible; adrenalectomy was carried out to palliate pain.

Metastatic cancer was identified in the adrenal glands of 24 (89%) of 27 patients with a current or prior history of renal cell carcinoma compared with 40% to 57% of those with a current or prior history of melanoma, colorectal cancer, prostate cancer, or non-small cell lung cancer. In 17 of 18 patients with adrenal metastasis who underwent

preoperative hormone evaluation, the results effectively excluded the presence of a functioning adrenal tumor. The remaining patient had a modest elevation in the 24-hour urine level of catecholamines, suggesting the possible presence of a pheochromocytoma; however, metastatic melanoma, not pheochromocytoma, was documented on final histopathologic evaluation of the patient's resected adrenal gland.

All 42 patients with adrenal metastases underwent preoperative cross-sectional imaging studies of the adrenal glands (CT and/or MRI). These studies showed characteristics suggestive of the presence of an adrenal metastasis rather than a primary adrenal tumor in 17 patients (40%). In the remaining 25 patients these studies could not reliably determine whether the adrenal masses were metastatic cancer or a primary adrenal neoplasm. Preoperative fine-needle aspiration (FNA) biopsy was performed in 18 patients (43%) and supported a diagnosis of metastatic cancer in 16 (89%) of the 18 patients.

In the 42 patients with an adrenal metastasis, the average time from initial cancer diagnosis to the diagnosis of adrenal metastasis was 3.9 years (median, 2.5 years; range, 0.0 to 14.9 years). After a median follow-up of 1.4 years, 19 (45%) of the 42 patients had died. The median actuarial overall survival duration after adrenalectomy was 3.4 years (Fig 1). This series included 2 patients who were alive more than 5 years after adrenalectomy; one had metastatic renal cell carcinoma, and the other had metastatic choriocarcinoma. There was no difference in survival duration between patients who underwent adrenalectomy for metastatic renal cell carcinoma and those who underwent adrenalectomy for non-renal cell carcinoma metastasis. Similarly, there was no difference in survival duration between patients who underwent adrenalectomy in the setting of prior or current extra-adrenal

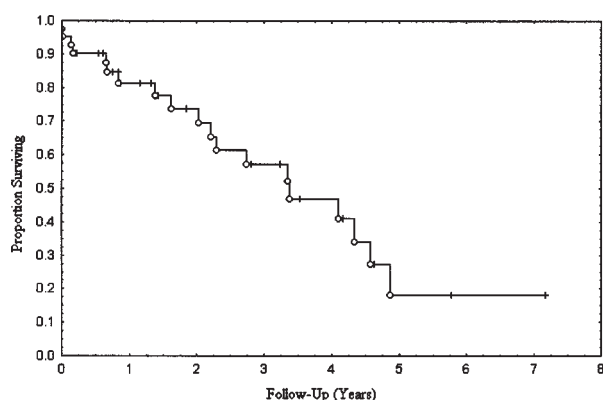


Fig 1. Kaplan-Meier disease-free survival curve for patients who underwent adrenalectomy for metastasis to the adrenal gland (n = 42; median follow-up, 1.4 years; median actuarial overall survival durations, 3.4 years). The overall survival duration is presented and calculated from the date of adrenalectomy.

distant metastatic disease and those whose distant metastatic disease was limited to the adrenal gland.

In 39 (48%) of the 81 patients the adrenal mass was a primary adrenal neoplasm (Table III). The median size of the resected primary adrenal tumors was 3.3 cm (mean, 4.4 cm; range, 0.8 to 20.0 cm). In this series the most common primary adrenal tumor was pheochromocytoma (19 patients, 49%); adrenal cortical adenoma was also frequently identified (13 patients, 33%). Fourteen of the 19 pheochromocytomas were identified in patients with multiple tumor syndromes, and the remaining 5 were sporadic. Bilateral pheochromocytoma was identified in 5 patients (all syndrome-associated). Primary cancer diagnoses associated with the presence of pheochromocytoma included medullary thyroid cancer (MTC) (11 patients, all with multiple endocrine neoplasia type 2 [MEN 2]) and melanoma (2 patients). Adrenal cortical adenoma was identified in patients with colorectal cancer, gastrointestinal stromal tumors, melanoma, non-small cell lung cancer, and cervical cancer (2 patients each). Two of 3 patients with adrenal cortical carcinoma¹⁰ had non-small cell lung cancer. The 2 cases of ganglioneuroma were identified in patients with melanoma.

Twenty-nine (74%) of the 39 patients with primary adrenal neoplasms underwent preoperative hormonal evaluation. The presence of a functioning adrenal tumor was confirmed in 19 patients (66%). Seventeen of these 19 patients had elevated levels of urinary catecholamines, confirming the presence of a pheochromocytoma; 1 patient had

Table III. Clinical characteristics of 39 patients with a history of cancer and an additional primary adrenal tumor process

Diagnosis of adrenal mass	No. of patients	No. of patients with bilateral adrenal masses
Pheochromocytoma	19	5
MEN 2	11	4
MEN 1 ²⁵	1	0
von Hippel-Lindau syndrome	1	1
Neurofibromatosis	1	0
Sporadic	5	0
Adrenal cortical adenoma	13	0
Adrenal cortical carcinoma	3	0
Ganglioneuroma	2	0
Nodular hyperplasia	2	1
Total (%)	39	6 (15)

an elevated level of urinary corticosteroids, and 1 patient had a plasma cortisol level that did not suppress in response to dexamethasone administration, confirming the presence of functioning adrenal cortical neoplasms. One patient with MEN 2 presented with an asymptomatic left adrenal mass; despite having normal 24-hour urine levels of total and fractionated catecholamines, adrenalectomy confirmed the presence of a pheochromocytoma. Of the 5 patients with sporadic pheochromocytomas, 4 had elevated preoperative levels of urinary catecholamines. The fifth patient was asymptomatic and did not undergo preoperative hormone evaluation; the results of preoperative imaging and FNA biopsy analysis were erroneously interpreted as suggestive of metastatic melanoma, as discussed below.

All 39 patients underwent preoperative CT scanning and/or MRI. These studies showed characteristics suggestive of a primary adrenal tumor rather than a metastasis in 10 patients (26%). Four patients with pheochromocytoma and 3 patients with adrenal cortical adenoma underwent confirmatory MRI, and 3 additional patients with pheochromocytoma underwent confirmatory metaiodobenzylguanidine imaging (MIBG). Preoperative FNA biopsy was performed in 11 patients (28%) but established a diagnosis of an additional primary adrenal tumor in only 3 (27%).

Case histories. The 4 case histories described below illustrate potential pitfalls in the evaluation of patients with an adrenal mass in the setting of a history of an extra-adrenal malignancy.

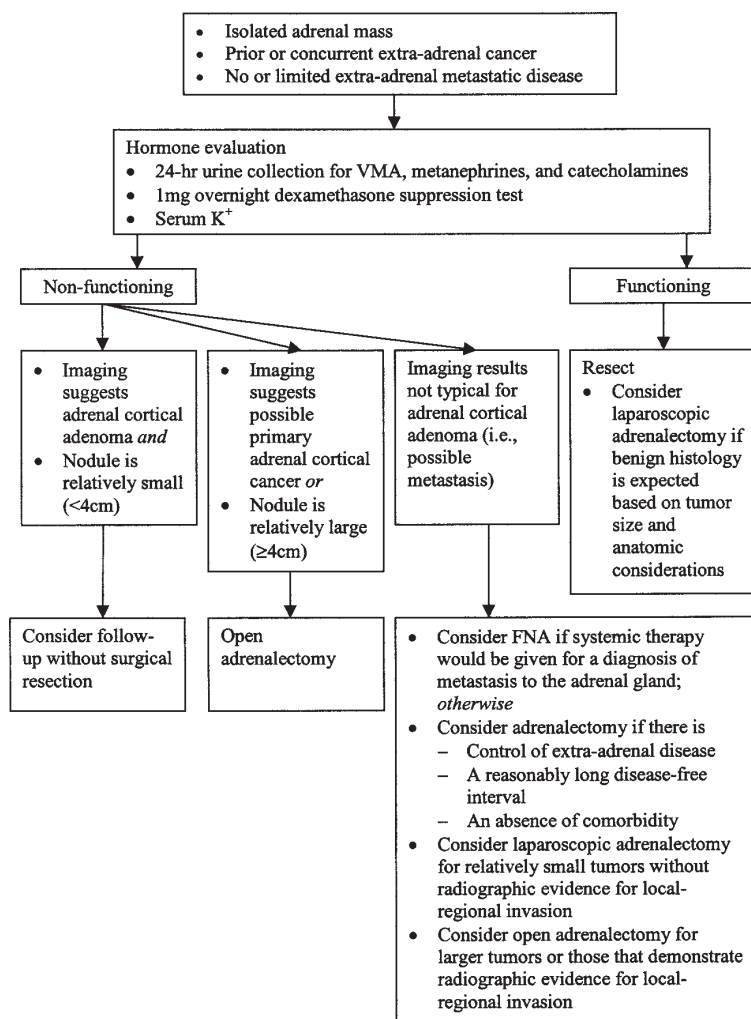


Fig 2. Algorithm for the evaluation and surgical treatment of patients with extra-adrenal cancer presenting with an adrenal mass. *VMA*, Vanillylmandelic acid.

Patient 1. A 42-year-old man with a history of regional nodal metastases from malignant melanoma was found to have a 3.9-cm left adrenal mass. Preoperative screening for hormone production was not performed. FNA biopsy of the mass was performed; a Fontana-Masson stain identified the presence of melanin; the biopsy findings were therefore believed to be consistent with metastatic melanoma. The patient underwent systemic therapy for metastatic melanoma without any change in the size of the mass; he subsequently underwent a left adrenalectomy. Intraoperative blood pressure lability suggested that the adrenal mass was a pheochromocytoma rather than metastatic melanoma. The final histopathologic analysis confirmed the diagnosis of a melanin-positive pheochromocytoma.

Patient 2. A 56-year-old man with a history of MTC and MEN 2 presented with a left adrenal mass. He had undergone a total thyroidectomy 10 years before referral. An evaluation for increasing carcinoembryonic antigen and calcitonin levels documented cervical nodal recurrence of MTC with associated hepatic metastases and a 3.5-cm

left adrenal mass. Preoperative imaging studies, including CT scanning and MRI, were nonspecific regarding the nature of the adrenal mass. The patient had no symptoms suggesting an excess level of catecholamines, and preoperative 24-hour urine collection showed that his level of total and fractionated catecholamines was normal. Given the high probability that the patient's tumor was a pheochromocytoma rather than metastatic MTC despite the normal catecholamine levels, adrenergic blockade was instituted. The patient subsequently underwent an uneventful laparoscopic left adrenalectomy. Final histopathologic analysis revealed that the adrenal tumor was indeed a pheochromocytoma.

Patient 3. A 43-year-old man with regional nodal metastases from melanoma was found to have a 3.2-cm left adrenal mass. He had no symptoms suggestive of a functioning adrenal tumor. However, 24-hour urine collection revealed elevated levels of dopamine (974 μg per 24 hours; normal, 100 to 440 μg per 24 hours) and total catecholamines (1006 μg per 24 hours; normal, < 540 μg per 24 hours). Although metastatic melanoma was still

Table IV. Reports of adrenal masses in patients with a history of an extra-adrenal malignancy

Study	Year	Type of study	Total no. of patients	No. of patients with an adrenal metastasis	No. of patients with a primary adrenal tumor	Percent of patients with a primary adrenal tumor
Present series	2001	Surgical	81	42	39	48
Saboorian et al ⁸	1995	FNA	161	80	81	50
Penn et al ¹²	1988	Surgical and observational	35	20	15	43
Belldegrun et al ¹³	1986	Surgical and observational	33	24	9	27
Total			310	166	144	46

considered a likely diagnosis, the patient underwent preoperative adrenergic blockade and subsequently underwent an uneventful laparoscopic left adrenalectomy. Final histopathologic analysis revealed that the mass was metastatic melanoma.

Patient 4. A 33-year-old man with a local recurrence of melanoma was found to have a 5.0-cm left adrenal mass. Preoperative screening evaluation revealed no evidence of a hormonally functioning adrenal tumor. CT characteristics of the mass were atypical for an adrenal cortical adenoma; because of the possibility that this represented metastatic melanoma, FNA was performed; this showed only cortical cells. The patient underwent surgical resection of his adrenal mass followed by that of his locally recurrent melanoma. The final histopathologic analysis of the adrenal mass revealed that it was a ganglioneuroma.

DISCUSSION

Relatively few studies have addressed the issue of appropriate evaluation and surgical treatment of adrenal masses in patients with a history of malignancy. Reports of adrenal incidentaloma often specifically exclude patients with synchronous or metachronous extra-adrenal malignancies,¹¹ whereas most reports of adrenalectomy for metastatic cancer exclude those with primary adrenal tumors.^{4,5} Table IV compares the present series with prior series that included patients with adrenal metastases from an extra-adrenal malignancy as well as those with unrelated primary adrenal tumors in the setting of a history of an extra-adrenal malignancy.^{8,12,13} These studies showed that the prevalence of primary adrenal tumors in patients with a history of extra-adrenal malignancy ranged from 27% to 50%. In the current series 48% of the patients found to have an adrenal mass in the setting of a previously or newly diagnosed extra-adrenal malignancy had a primary adrenal tumor. When patients with syndrome-associated pheochromocytoma were excluded, primary adrenal tumors were still identified in 37% of the patients (25 of 67).

In the current series, malignancies that metastasized to the adrenal gland included renal cell car-

cinoma, melanoma, colorectal cancer, prostate cancer, and non-small cell lung cancer. Metastasis to the adrenal gland is a more likely cause of an adrenal mass in patients with a history of these malignancies.^{3-5,12-14} However, not all patients with these malignancies will have adrenal metastases.⁶ Patient 1 illustrates this concept; an FNA biopsy of the adrenal mass in this patient was erroneously interpreted as demonstrating metastatic melanoma rather than pheochromocytoma. As occurred in this patient, pheochromocytoma may express melanin and therefore be confused with metastatic melanoma on cytologic evaluation of an FNA specimen.¹⁵ Patients with an extra-adrenal malignancy and adrenal mass should undergo a standard hormone evaluation, including a timed urine collection for measuring the level of catecholamines, before FNA biopsy or surgical resection.

Although the overall prognosis for patients with metastatic cancer in the adrenal glands is poor,⁷ the survival duration in highly selected patients who undergo adrenalectomy for metastatic cancer^{3-5,14,16} is similar to that in patients who undergo resection of metastases in other visceral sites, such as the liver¹⁷ and lung.¹⁸ It seems reasonable to apply similar criteria for selecting patients for resection of adrenal metastases,^{17,18} including control of extra-adrenal disease, a reasonably long disease-free interval, an acceptable patient performance status, and the absence of significant comorbidity. Recommendations regarding evaluation and treatment of patients presenting with an adrenal mass in the setting of extra-adrenal cancer are summarized in Fig 2.

Although a screening hormone evaluation is an essential part of the evaluation for all patients with an adrenal mass, the limitations of this screening must be recognized.^{19,20} As illustrated by patient 2, urinary catecholamine levels may occasionally be normal in MEN 2 patients with small pheochromocytomas.¹⁹ MIBG may assist in confirming the diagnosis in such patients.²⁰ Alternatively, as seen in patient 2, adrenergic blockade followed by surgical resection can be performed without MIBG confir-

mation if cross-sectional imaging studies suggest the diagnosis of pheochromocytoma.

In contrast to the false-negative urinary screening result obtained in patient 2, patient 3 illustrates that modest elevations of urinary catecholamine levels can be a nonspecific finding. Patients with metastatic melanoma in particular may have elevated urinary dopamine levels, most likely because of increased conversion of tyrosine to the dopamine precursor L-dopa by tyrosinase in melanoma tumor cells.²¹ Although MIBG imaging might be considered in the evaluation of such patients, results from MIBG imaging must be interpreted with caution in patients with possible adrenal metastases from tumors of neural crest origin, such as melanoma, because these tumors may accumulate MIBG.²² An appropriate treatment strategy for these patients may include preoperative adrenergic blockade, even if the clinical scenario suggests that the likelihood of pheochromocytoma is relatively low.

Finally, patient 4 illustrates the complex management issues often faced by patients with extra-adrenal malignancy and an adrenal mass. This patient underwent pretreatment screening for hormone production. After documentation of normal hormone levels, treatment planning for his recurrent melanoma required FNA biopsy of his adrenal mass to determine whether distant metastatic disease was present. These biopsy findings revealed only cortical cells and were therefore nondiagnostic; CT findings were not typical of adrenal cortical adenoma.²³ Therefore, surgery was recommended. First, an adrenalectomy was performed. When this procedure identified a second primary tumor (ganglioneuroma) rather than metastatic melanoma, aggressive surgical treatment of the patient's locally recurrent melanoma was performed. This procedure consisted of wide local excision of the melanoma site with myocutaneous free-flap coverage as well as intraoperative lymphatic mapping and sentinel lymph node biopsy to provide surgical staging of the patient's regional nodal basin.²⁴

In summary, patients with extra-adrenal cancer and an adrenal mass frequently have an adrenal pathologic condition independent of their primary malignancy. Despite the presence of a newly diagnosed malignancy or the history of a malignancy, all patients with an adrenal mass should undergo a standard hormone evaluation to confirm that the mass is not a functional neoplasm. An assumption that the adrenal mass is metastatic disease will be wrong in up to half of such patients.

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DISCUSSION

Dr Paul Gauger (Ann Arbor, Mich). This is an excellent paper with a very important message. I have an inherited abhorrence for FN biopsy of the adrenal, but certainly this is one of the settings in which one commonly sees it done, a history of malignancy elsewhere. I am curious about how the use of needle biopsy factored into the patients in this study, and how you would reconcile the use of that now that you have shown us that so many of these lesions are actually not metastases. Certainly pursuing that practice of needle biopsy is going to be dangerous in the setting of a pheochromocytoma.

Dr Lenert. We emphasize that hormone screening to exclude pheochromocytoma must be performed before FNA to avoid the error in diagnosis and management illustrated in the first case presented. We would generally consider an FNA only when the findings would change the management of the patient. For example, we would consider FNA of a nonfunctioning adrenal mass in a patient with a history of cancer whose imaging studies suggest a possible metastasis to the adrenal gland, if systemic therapy would be given for a diagnosis of metastasis to the adrenal gland.

Dr Gauger. More of your patients underwent open adrenalectomy. I wonder how much of that represents the fact that during the study period, the preferred operation changed as laparoscopic technology was incorporated only toward the end of the study period. Or, was it a conscious choice that in most of these cases you were

avoiding laparoscopic adrenalectomy for suspected malignant disease?

Dr Lenert. You are correct in that the majority of patients in the current series underwent adrenalectomy before the availability of selective laparoscopic adrenal resection. Currently we would consider a laparoscopic approach for patients in whom benign histology is expected (based on tumor size and anatomic considerations) and for patients with suspected metastases to the adrenal gland with modestly sized tumors that do not show radiographic evidence for local-regional invasion.

Dr Michael McLeod (Kalamazoo, Mich). This will take you maybe just a little bit off your main theme. I agree with you that it is important to evaluate these adrenal lesions hormonally before excising them in the context of the concern about potentially missing subclinical hyperfunction or subclinical Cushing's. This allows you to make a decision about whether you have to cover the patient with perioperative cortisol. Would you share with me what is your minimal workup for ruling out an occult hyperfunctioning cortisol-producing tumor that clinically is not apparent but may be associated with suppression of the contralateral gland? In summary, what would be your minimal workup to rule out abnormal cortisol function in these lesions?

Dr Lenert. We recommend that hormone screening for patients presenting with an isolated adrenal mass in the setting of prior or concurrent extra-adrenal cancer consist of a 24-hour urine collection for vanillylmandelic acid, metanephrines, and catecholamines, a 1-mg overnight dexamethasone suppression test, and a serum potassium level.

Dr Charles Proye (Lille, France). I think that in such cases, for diagnosis or exclusion of diagnosis of pheochromocytoma, rather than free catecholamine measurement, I would advocate measurement of urinary and plasma methoxyderivatives, which are much more sensitive tests.

Dr Janice Pasiaka (Calgary, Alberta, Canada). The surgical dogma would say that bilaterality is something that we should be looking for when looking at metastatic disease. Could you tell us whether bilaterality at all predicted in these patients whether mass was metastatic or nonmetastatic?

Dr Lenert. There were 10 patients in this series who had bilateral disease. Four had bilateral adrenal metastases. The other 6 patients had benign histology: 5 had bilateral pheochromocytomas and 1 had bilateral nodular hyperplasia.