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Management of suspected adrenal metastases at 2 academic medical centers

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Abstract

BACKGROUND: The optimal management of suspected adrenal metastases remains controversial.

METHODS: This is a retrospective bi-institutional review of 37 patients who underwent adrenalectomy for suspected adrenal metastasis between 2001 and 2014.

RESULTS: Three (8%) patients had benign adenomas on final pathology. At a median follow-up of 21 months, 7 (32%) patients were alive with no evidence of disease and 7 (32%) were alive with recurrent disease. Recurrence-free survival (RFS) was 8 months; decreased RFS was associated with positive margins and size $\geq$6 cm. Overall survival (OS) was 29 months; decreased OS was associated with capsular disruption. There were no differences in RFS or OS by surgical approach.

CONCLUSIONS: The favorable OS supports adrenalectomy in select patients with suspected adrenal metastases. Minimally invasive adrenalectomy is safe and effective, but the surgical approach should be based on the ability to achieve a margin-negative resection with avoidance of capsular disruption.

Benign cortical adenomas are the most common type of adrenal tumor.[1] However, in patients with a history of extra-adrenal malignancy, approximately half of resected adrenal tumors are found to be metastases.[2,3] Similarly, up to 38% of patients who die from an extra-adrenal malignancy are found to have adrenal metastases at autopsy, suggesting that the adrenal gland is one of the most common sites for metastasis.[4–7] Although adrenal metastases from other primary malignancies have been described, non–small cell lung cancers, melanomas, and renal-cell carcinomas account for most reported cases; this is likely because of the adrenal gland's rich sinusoidal blood supply and possible communication between pulmonary and retroperitoneal lymphatics.[6–9]

According to recent guidelines from the American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons, adrenal metastectomy may be considered in select patients.[10] For adrenalectomy to confer the greatest benefit to recurrence-free survival (RFS) and overall survival (OS), multiple reports have suggested that extra-adrenal disease should be adequately controlled, metastases should be isolated to, and confined within, the

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adrenal gland, and patient performance status and life expectancy should warrant surgical intervention.[11–13] Additional factors that have been associated with an improved OS include metachronous (rather than synchronous) solitary tumors, disease-free interval (DFI) greater than 12 months from the time of primary tumor diagnosis, tumor size less than 4.5 cm, and metastases from renal cell carcinoma (as opposed to other primary tumors).[12,14–16]

The optimal evaluation and management of adrenal metastases, including the role for biopsy and minimally invasive resection, remain controversial, as retrospective single-institution studies account for most reported patients.[12,17,18] A recent systematic review, which assessed 30 retrospective studies and over 800 patients, concluded that adrenalectomy was associated with a prolonged median OS when compared with chemotherapy or targeted therapy alone; however, the authors noted significant selection bias in the published studies and could not comment on the role of biopsy or the optimal surgical approach.[18] Most current studies do not report important data related to disease presentation, preoperative patient evaluation, or the use of the posterior retroperitoneoscopic approach for suspected adrenal metastases.[3,17,18] Therefore, the aim of this study was to describe the presentation, evaluation, and outcome data for patients who underwent adrenalectomy for suspected adrenal metastases at 2 academic medical centers, where minimally invasive adrenalectomy has now become the standard of care for benign and metastatic adrenal disease.

Methods

This is a retrospective review of 2 prospectively collected adrenal databases, which included a total of 458 adrenalectomies performed between 2001 and 2014 at 2 academic medical centers. Adult patients ($\geq$18 years) with previously diagnosed primary malignancies who underwent adrenalectomy for suspected adrenal metastases were included for analysis. We excluded patients who underwent en bloc adrenalectomy at the time of another tumor resection (ie, renal cell carcinoma) and those who underwent palliative or debulking procedures without curative intent. Demographic and clinical data, including preoperative evaluation (medical history, physical examination, computed tomography [CT], 18F-fluorodeoxyglucose positron emission testing [FDG-PET], biochemical analysis, biopsy results, and preoperative systemic therapy), operative findings, pathological review, perioperative outcomes, and follow-up data, were collected. Synchronous and metachronous adrenal metastases were defined by a 6-month cutoff from the time of primary tumor diagnosis–synchronous being less than 6 months from the date of original cancer diagnosis and metachronous being 6 months or longer.

All patients underwent preoperative cancer staging, which included cross-sectional imaging of the head, chest, abdomen and/or pelvis, and in most instances, adrenal protocol CT. FDG-PET was used as a diagnostic and staging adjunct but was not routinely performed in all patients. Biochemical evaluation was performed in all patients to assess for functionality of the adrenal tumor. Although this evaluation varied slightly between the 2 institutions, it included assessment for hypercortisolism (low-dose dexamethasone suppression testing, salivary cortisol, and/or 24-hour urine cortisol levels), primary aldosteronism (serum aldosterone and renin levels), and pheochromocytoma (fractionated serum metanephrine and/or 24-hour urinary metanephrine levels). Adrenal biopsy was not routinely performed at either institution; however, when it was performed, image-guided percutaneous fine-needle aspiration was the method of choice.

Adrenalectomy was considered for patients with suspicion of isolated adrenal metastases in the absence of extra-adrenal disease, or in rare cases, for oligometastases when the site of extra-adrenal disease was considered to be stable and low volume. Open resection was the favored surgical approach early in the study period, however, with the gradual adoption of minimally invasive techniques at both institutions, open adrenalectomy became reserved for select patients based on body habitus, tumor size, proximity to vital structures, and anticipated difficulty of dissection. The choice of minimally invasive approach (laparoscopic transabdominal or posterior retroperitoneal) was at the surgeon's discretion but was largely dependent on patient body habitus, comorbidity, and prior surgical procedures; both techniques are commonly performed at both institutions.

DFI was defined as the period of time between primary tumor diagnosis and adrenal metastasis diagnosis. RFS was defined as the period of time from adrenalectomy to the date of disease recurrence or death, whichever occurred first. OS was defined as the time from adrenalectomy to the date of death from any cause. Continuous variables were evaluated using *t*-tests, and categorical variables were analyzed with chi-square tests. Log-rank tests, Cox proportional hazard models, and Kaplan–Meier survival curves were used to evaluate associations between clinical variables, RFS, and OS data. All analyses were unadjusted and performed with STATA version 13.0 (StataCorp, College Station, TX), and a *P*-value of less than .05 was considered statistically significant.

Results

Of the 458 adrenalectomies performed during the study period, 37 (8%) were for suspected adrenal metastases; median age was 64 years, and 19 (51%) were male. The most common primary malignancies were non–small cell lung cancer (12, 32%), melanoma (7, 19%), colorectal cancer (5, 14%), and renal cell carcinoma (4, 11%; Table 1). The primary malignancies were treated before adrenalectomy with either surgery alone (18 of 37, 49%), surgery plus chemotherapy (8, 22%), surgery plus chemoradiation (7, 19%), chemotherapy alone (2, 5%), or