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ORIGINAL ARTICLE

Adrenal surgery for oligometastatic tumors improves survival in selected cases

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KEYWORDS
Adrenalectomy;
Adrenal metastasis;
Oligometastatic;
Prognostic factor;
Predictive factor

Summary
Introduction: Oligometastatic cancer prognosis is distinct from polymetastatic cancer prognosis and surgery can improve survival. The objective of this study was to assess the role of adrenalectomy and to look for prognostic or predictive factors for the treatment of patients with oligometastatic solid tumors and adrenal metastasis.
Material and methods: Patients with oligometastatic solid tumors undergoing adrenalectomy were selected. Clinical data were retrieved from electronic patients records. Progression-free survival (PFS), overall survival (OS) and clinical outcomes were assessed.
Results: Forty patients were analyzed. Median PFS was 7.4 months and PFS was longer for metachronous versus synchronous adrenal metastasis (10.8 versus 4.5 months; $P=0.008$). Median OS was 22.8 months and OS was better with laparoscopic adrenalectomy versus open adrenalectomy (24.4 versus 11.2 months; $P=0.05$).
Discussion: Adrenalectomy part of the treatment plan of oligometastatic solid tumors but patients have to be selected. Surgery might be indicated for metachronous metastasis when laparoscopic adrenalectomy is possible.

Introduction

The majority of patients diagnosed with solid tumors has metastasis at the time of diagnosis or will develop metastasis during the course of disease [1]. Oligometastatic cancers are defined as solid tumors with up to 5 metastases [2]. Clinical and biological data support the hypothesis that oligometatic disease is a specific entity, distinct from early-stage disease and polymetastatic disease [3]. As an example, in the 8th edition of the TNM classification of lung cancer, a new category of patients with a single metastasis (M1b) was individualized as their prognosis was distinct from patients with multiple metastases [4]. Genetic and

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epigenetic factors enable cancer cells to spread in specific organs following the ''seed and soil'' theory [5]. As olimetastatic diseases usually progress into polymetastatic diseases, it has been shown that better local control improves systemic control of the disease. Surgery of metastases can indeed improve survival [6,7]. In particular, for non-small cell lung cancer brain metastasis, patients undergoing bifocal surgery had a longer median survival than patients receiving palliative therapy (23.12 versus 10.3 months, respectively) [8]. In a series of autopsied cases of patients with solid tumors, adrenal glands were a frequent site of metastasis (27%), especially for patients with breast and lung carcinoma (53.9 and 35.6%, respectively) [9]. With the improvement of adrenal imaging, adrenal gland metastasis diagnosis can be made earlier [10]. No randomized study has been conducted to assess the role of adrenal gland metastasis surgery for patients with oligometastatic solid tumors and there is no guideline in this field. The primary objective of this study was to report the outcomes of patients with oligometastatic solid tumors undergoing adrenal metastasis surgery. The secondary objective was to look for potential prognostic or predictive factors to guide the treatment of these patients.

Material and methods

Patients

Patients with histologically proven solid tumor with adrenal metastasis treated in our institution from September 1994 to September 2012, registered as C797 using the International Classification of Disease for Oncology site, were identified. Preoperative tests were performed, including brain, chest and abdomen CT scan and blood tests (cortisol, ACTH). Patients with non-secreting adrenal metastasis and with oligometastatic tumor (up to 5 metastases found in up to 2 organs) who underwent adrenalectomy were selected for the study. The term oligometastatic thus included either patients with solitary adrenal metastasis or patients with adrenal metastasis and other metastatic sites. Patients were enrolled if the other metastases were also resected.

Ethics

The protocol was submitted to and approved by our institution ethics committee (Commission Informatique et Libertés [CIL]). All patients gave their consent for the retrieval of de-identified clinical, pathological and biological data prior to adrenal gland surgery.

Data retrieval

For each patient, clinical data (age, sex, pathology, date of diagnosis, date of surgery, relapse, date of death or last follow-up) were retrieved from the electronic patient record. We also collected data regarding adrenal metastasis: date of diagnosis, size, type of surgery, resection margins (R0: tumor free; R1: microscopic invasion; R2: macroscopic invasion; Rx: unknown) and adjuvant therapy. Adrenal metastasis was considered as synchronous if diagnosed less than 6 months after primitive tumor diagnosis and was considered as metachronous if diagnosed more than 6 months after primitive tumor diagnosis.

Progression-free survival (PFS) was calculated from the date of adrenalectomy to the date of relapse or death or last follow-up. Overall survival (OS) was calculated from the date of adrenalectomy to the date of death or last follow-up.

Statistics

Statistical analyses were performed using the SSPS software, version 17. Survival curves were drawn using Kaplan-Meyer technique and were compared using log-rank test. Chi^2 test was used to compare clinical outcomes in different subgroups. Difference was considered as significant when P-value < 0.05.

Results

Patients

A total of 40 patients 65% men and 35% women with oligometastatic solid tumors treated with adrenalectomy from September 1994 to September 2012 were selected. Patients' clinical characteristics are reported in Table 1. The median age was 57-year-old. A majority of patients had lung cancer (52.5% versus 20% renal cell carcinoma and 27.5 other primitive tumors) and metachronous adrenal gland metastasis (72.5% versus 27.5% synchronous metastasis). The mean size of adrenal metastasis was 60 mm. The therapeutic decision was made after multidisciplinary tumor board discussion. Most patients underwent laparoscopy (75% versus 25% laparotomy). In 17.5% cases, laparoscopy had to be converted into laparotomy. After surgery, resection margins were free of disease (R0) in 65% cases versus 5% microscopic tumor invasion (R1) and 12.5% macroscopic tumor

Table 1 Patients' demographic characteristics.

Demographic	*n* (%)
Sex	
Male	26 (65)
Female	14 (35)
Median age	57
Primitive tumor	
Lung	21 (52.5)
Renal cell carcinoma	8 (20)
Other	11 (27.5)
Adrenal metastasis	
Metachronous	29 (72.5)
Synchronous	11 (27.5)
Surgery	
Laparoscopy	30 (75)
Laparotomy	10 (25)
Conversion to laparotomy	
Yes	7 (17.5)
No	33 (82.5)
Resection margins	
R0	26 (65)
R1	2 (5)
R2	5 (12.5)
Rx	7 (17.5)
Adjuvant chemotherapy	
Yes	24 (60)
No	16 (40)

R0: tumor free; R1: microscopic invasion; R2: macroscopic invasion; Rx: unknown.