

Case Report

Metastatic Renal Cell Carcinoma: Don't Dismiss the Surgeon

Elisa Cassiers and Pol Specenier*

Department of Oncology, Antwerp University Hospital, Wilrijkstraat 10, 2650 Edegem, Belgium

*Corresponding author: Pol Specenier, Department of Oncology, Antwerp University Hospital, Wilrijkstraat 10, 2650 Edegem, Belgium, E-mail: pol.specenier@uza.be

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Abstract

We present a case illustrating that even in the era of new systemic therapies, surgery can still play an important role in the management of metastatic RCC, provided that patients are carefully selected. In these patients, repeated surgical removal of metastases can be associated with a prolonged survival and excellent quality of life.

Keywords: Surgery; Metastatic Renal Cell Carcinoma

Introduction

Renal cell carcinoma (RCC), which originates from the renal cortex, represents 2-3% of all carcinomas. It is the most common solid tumour of the kidney, and accounts for approximately 90% of all primary renal neoplasms. It occurs about 50% more often in men compared to women, and has a peak incidence between the ages of 60 and 70 years [1].

Three major histopathological subtypes of RCC have been defined by the World Health Organisation, based on histological and genetic characteristics: Clear cell (ccRCC), which accounts for 80-90 % of cases and which commonly exhibits a deletion of chromosome 3 and a mutation in the Von Hippel-Lindau gene (VHL), Papillary (10-15% of RCCs), which is further divided into two subtypes according to the size of the cells and features of the cytoplasm and which is frequently associated with trisomies and loss of the Y chromosome, and Chromophobe (4-5% of cases), which is associated with a combination of loss of different chromosomes [1-3]. Squamous cell carcinomas of the renal pelvis are rare (0,7-7%). They are strongly associated with chronic renal calculi, but also with phenacetin consumption, pyelonephritis and squamous metaplasia [4]. There have been different reports on atypical presentations of this rare malignancy, including hydronephrosis, and a solid mass in a horseshoe kidney with associated renal stones [4-6]. Renal cell carcinoma has a strong propensity to metastasize, and about 20-30% of patients will already have metastases at presentation [7,8]. The most common distant site is the lung, but metastases also occur in bone, brain, adrenal gland and liver. More uncommon sites of metastasis include the pancreas, thyroid gland, perinasal sinuses, large intestine and bladder [7,8].

Atypical presentations at diagnosis are not rare. For example, Vasev et al. reported on a patient with a painless, pulsatile sternal metastasis as first presentation of renal cell carcinoma [9].

Prognosis of untreated, metastasized RCC is poor, with a 5-year survival rate between 0-10%. Mean survival is about 7-12 months [1,7,8].

Recently, multiple systemic targeted agents have shown to improve the outcome of patients with metastatic RCC. However, surgery should not be dismissed as an important therapeutic option

for patients with metastatic RCC, as illustrated by our case report.

Case Description

A 46-year old Caucasian male was diagnosed with clear cell carcinoma of the right kidney in February 2005, for which a radical right nephrectomy was performed. His subsequent surgical history is summarized in the below (Table). On 6 different occasions, metastases in the lungs and brain were surgically removed, during which the patient managed to hold an excellent performance status.

Date	Surgical intervention	Findings
September 2005	Median sternotomy	Bilateral lung metastases
March 2007	Lobectomy left superior lobe	Left lung metastases (multiple)
June 2007	Metastasectomy right lung	Right lung metastases (multiple)
August 2008	Metastasectomy right lung	Right lung metastases (4)
November 2010	Metastasectomy brain	Solitary metastasis right frontal lobe
July 2013	Metastasectomy right lung	Right lung metastases (2)

In November 2013, PET- scan showed a new solitary metastasis in the right upper lung lobe. Right pneumonectomy was unfortunately impossible, due to inadequate left pulmonary function. No treatment was started as the patient was asymptomatic. In April 2014 however, manifest tumour progression was observed and sunitinib 50 mg/day 4 weeks on, 2 weeks off, was started. Unfortunately, the treatment was poorly tolerated (loss of taste, asthenia, severe hand-foot syndrome). At re-evaluation in August 2014, tumour progression in the lungs and lymph nodes was documented. In the same month, the patient was admitted after a seizure with 7th nerve paresis. MRI of the brain showed a new solitary metastasis with intralesional hemorrhage and perilesional edema in the right frontal lobe. The brain metastasis was also resected. Subsequent second line systemic treatment has been started but is also poorly tolerated.

Resection of RCC metastases: literature data

Several studies have reported 5-year survival rates after solitary metastasectomy of 29% to 35%, but outcome depends on various factors, such as patient performance status, site of metastasis, interval after nephrectomy, presence of solitary or multiple metastases and possibility of complete resection [7,10-13]. A recent study conducted

at the University of Texas M.D. Anderson Cancer Center [11] described the cases of 179 patients who were known to have metastatic RCC between 1984 and 1997 and who underwent resection for an apparently solitary metastatic lesion. Reported sites of metastasis were the lung (N=50), axial bone (N = 29), appendicular bone (N= 27), visceral organs (N= 23), brain (N= 23), locoregional (including renal fossa or regional lymph nodes, N= 17) and skin (N= 10). Overall 5-year survival was 29%, but survival rates varied according to the site of metastasis: 56% for lung, 49% for locoregional, 28% for skin, 20% for visceral organ, 18% for appendicular bone, 13% for brain and only 9% for axial bone metastasis. In general, patients with a metachronous solitary metastasis fared better as compared to a synchronous metastasis (5-year survival of 39% and 22%, respectively). These results support surgical resection as a therapeutic option in patients with solitary metastasis.

Resection of multiple metastases has also been reported in many studies for various sites. In the aforementioned study at the M.D. Anderson Cancer Center [11], 60% of patients who developed recurrent disease after prior resection of a lung metastasis were able to undergo subsequent resection. Predictors of adverse outcome in terms of disease-free interval and overall survival include a high nuclear grade according to Fuhrman (especially sarcomatoid histology), synchronous metastases or a short disease-free interval after nephrectomy, metastatic sites other than the lung (especially liver and brain) and multiple organ site involvement [11-13]. These factors plead for a more careful patient selection and can be arguments against aggressive surgical treatment.

Resection of lung metastases

Reported 5-year survival rates after lung metastasectomy vary from 21-60%, which is significantly higher than reported rates for untreated patients (3-11%) [7,11-14]. Evidently, complete resection should be attempted, while preserving adequate pulmonary function.

Favourable prognostic factors include the possibility of complete resection, solitary lung lesions instead of multiple lesions, absence of metastatic regional and mediastinal lymph nodes and a long disease-free interval from nephrectomy to diagnosis of pulmonary metastases [7,11,12,14]. Open surgery, has been commonly recommended, as it allows intra-operative palpation of eventual small metastases not yet visible on computed tomography. However, more and more centers are gaining expertise in thoracoscopic techniques for resection of pulmonary metastases [7].

A single-institution retrospective study, conducted at the Osaka Medical Center for Cancer and Cardiovascular Diseases [12], described the cases of 48 patients who underwent thoracotomy for RCC lung metastases. Cumulative 3-, 5- and 10-year survival rates were 60%, 47% and 18% respectively. Several factors were found to be significantly related to survival: disease-free interval (5-year survival rate of 58% for DFI >2 years and 26% for DFI <2 years), number of resected metastases (55% for solitary and 37% for multiple metastases) and completeness of resection (50% for complete resection and 20% for incomplete resection).

Resection of brain metastases

Brain metastases from RCC account for 4-10% of all metastatic sites of RCC [7,15,16]. Most brain metastases occur when the

patient already has extra-cranial disease, and they are almost always symptomatic due to large amounts of peritumoural edema, spontaneous intra-cranial bleeding and associated neurological symptoms. Untreated, patients with brain involvement seldom survive longer than a few months [7,11,15-17]. Surgical removal of RCC brain metastases will not only offer symptom relief but can also be a curative option if complete resection is possible [7,11,13,15-17].

Wronski [17] analyzed 50 patients who were treated with craniotomy for RCC brain metastases. Reported survival time from craniotomy was 12 months, with no difference between patients with solitary or multiple lesions. Sheehan [16] reported on a series of 69 patients treated for RCC brain metastases by means of STRS. Local tumour control was achieved in the majority of patients, confirmed by post-operative imaging. Overall median survival was 15 months from diagnosis of brain involvement and 6 months from radiosurgery.

Conclusion

Our case illustrates that even in the era of new systemic therapies, surgery can still play an important role in the management of metastatic RCC, provided that patients are carefully selected. In these patients, repeated surgical removal of metastases can be associated with a prolonged survival and excellent quality of life.

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