

Nine-year survival after iterative metastasectomies for renal cell carcinoma

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Abstract

We report the case of a 24-year-old male, diagnosed with an incidental T3a papillary renal cell carcinoma (RCC), treated with left laparoscopic radical nephrectomy. After 7 months, nodal recurrence was identified and retroperitoneal lymph node dissection (RPLND) was performed. Four months later, due to local recurrence, the patient underwent salvage RPLND, partial psoas resection and left adrenalectomy, and remained without recurrence during the following 15 months, after which treatment with sunitinib was started due to multiple metastases in pelvic lymph nodes, lungs, and bone. After 4 years of stable disease, progression at the quadratus lumborum and psoas muscles led to subsequent metastasectomy. No evidence of progression was identified for 2 years, after which, despite multimodal treatment (axitinib and radiotherapy to bone lesions), widespread disease progression led to patient death. This uncommon case of prolonged survival with metastatic RCC highlights the possible role of iterative metastasectomies in the management of advanced stage disease, as well as its potential to extend the survival substantially, even when progressive on tyrosine kinase inhibitors.

Keywords: Metastasectomy, metastases, mortality, renal cell carcinoma, tyrosine kinase inhibitor

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INTRODUCTION

The presence of metastasis is the most significant negative prognostic factor in renal cell carcinoma (RCC).^[1] Due to the relatively reduced effect of systemic agents in metastatic RCC, even with the advent of targeted immunotherapy, over the past years, there has been a growing interest on the possible effect of metastasectomies in the progression-free and cancer-specific survival of patients with metastatic RCC.^[1]

CASE REPORT

A 24-year-old asymptomatic male, without relevant medical or family history, was diagnosed with a 5-cm solid lesion

on the left kidney on routine abdominal ultrasound. The patient underwent left laparoscopic radical nephrectomy in May 2006. Pathology of the nephrectomy specimen revealed pT3a papillary RCC, with negative surgical margins.

Five months after, the patient presented with asymptomatic nodal recurrence on fluorodeoxyglucose positron-emission tomography/computed tomography (FDG-PET/CT). Laparoscopic metastasectomy was attempted, but pathology of the specimen was negative. Two months later, open retroperitoneal lymph node dissection (RPLND) was performed. Pathology of the specimen revealed

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papillary RCC metastasis on one lymph node, with capsular perforation. Five months later, recurrence at the nephrectomy fossa was detected with FDG-PET/CT. The patient was referred to our center and underwent salvage open left para-aortic RPLND, partial psoas resection, left adrenalectomy, and partial colectomy. Pathology of the specimen revealed 5/15 positive nodes.

The patient remained recurrence-free for 15 months, after which multiple metastases were identified at the level of the left quadratus lumborum muscle, common iliac and external iliac lymph nodes, lungs, and vertebral body L3. Therapy with sunitinib was started, with favorable response.

In January 2013, after 37 cycles of sunitinib, although the pulmonary nodules remained stable, there was progression at the level of the left quadratus lumborum and psoas muscles, and a subsequent metastasectomy was undertaken. A partial resection of the psoas and quadratus lumborum muscles was performed, after which treatment with sunitinib was resumed.

In January 2015, after a total of 52 cycles of sunitinib, widespread progression of disease was identified, with substantial bone involvement, and treatment with axitinib and radiotherapy of spinal and iliac lesions (39 Gy in 13 fractions) was implemented. Despite the multimodal approach, the patient died in May 2015, due to disease progression, at the age of 33.

DISCUSSION

RCC is one of the most common malignancies nowadays, with recent studies showing it was the sixth most frequently diagnosed malignancy and the 10th most frequent cause of death by cancer in Europe in 2012.^[2] Due to the widespread use of abdominal imaging, most RCCs are identified while still asymptomatic and localized.^[1] However, the presence of advanced disease (T3–4, N+, and M+) at the time of diagnosis varies from 16.9% to 28%, according to the histological subtype.^[1] To date, surgical treatment remains the recommended treatment option for localized RCC.^[1] The patient presented with an incidental cT1b kidney tumor, without evidence of local, nodal, or metastatic extension, and was, therefore, treated with surgery with curative intent.

Isolated local recurrence of RCC after radical nephrectomy is uncommon, with most cases occurring in patients with locally advanced disease, even in the presence of negative surgical margins.^[3] More than 64% of patients with local recurrence are asymptomatic, which is why adequate

follow-up programs in high-risk patients are essential.^[1,3] More than 35% of local recurrences occur on RPLNDs.^[3] Early local recurrence on regional lymph nodes may be difficult to differentiate from normal postoperative features on conventional imaging. Our patient presented with early asymptomatic local recurrence in the regional lymph nodes, diagnosed on FDG-PET/CT.

In the presence of isolated local recurrence, surgical resection is associated with median recurrence-free and cancer-specific survival periods of 11 and 61 months, respectively.^[3] In the absence of higher-quality scientific evidence, surgical resection of isolated local recurrence is currently recommended.^[1] The quality of surgery for local recurrence is of paramount importance, considering that positive surgical margins are an independent risk factor for cancer-specific survival.^[3] In our patient, unsuccessful laparoscopic RPLND was performed, followed by open RPLND, with confirmatory pathology of local recurrence. In the presence of an FDG-PET/CT compatible with a second recurrence in the nephrectomy fossa, the patient was referred to our center and underwent wide salvage RPLND, remaining recurrent-free for >1 year.

The appearance of metastasis constitutes the most important factor associated with cancer-specific mortality in RCC after surgical treatment with curative intent, with 5-year survival rates being as low as 8%.^[4,5] Systemic conventional immunotherapy and cytotoxic chemotherapy have shown little to no activity in metastatic RCC (mRCC), while causing considerable toxicity.^[5] Systemic therapy with targeted agents, namely, tyrosine-kinase inhibitors (TKIs), was a paradigm shift in the treatment of mRCC.^[4,5] First-line targeted therapy with sunitinib has revealed a significant improvement in median overall survival when compared to interferon alfa, with a more favorable pattern of side effects.^[6] In the specific subset of patients with papillary mRCC, treatment with sunitinib was associated with an improvement of the overall radiographic response, when compared to everolimus.^[7] For this reason, treatment with sunitinib is nowadays considered as first-line therapy for mRCC of all histological subtypes.^[1] A comparison of the survival rates of patients with mRCC, between the pretargeted and the targeted therapy eras, has shown a significant improvement of both cancer-specific and all-cause mortality.^[8] Nonetheless, mRCC remains an aggressive malignancy and complete remission is rare (1%–3%) using systemic therapy alone. Surgical resection of the primary tumor and metastatic deposits continues to play an important role in managing mRCC patients.^[1] Complete surgical resection of metastasis appears not only to provide palliation but also to prolong progression-free

and cancer-specific survival, regardless of the subsequent use of systemic therapy.^[9,10] In fact, the quality and completeness of metastasectomy is clearly an independent factor associated with the overall survival, regardless of the number and location of the lesions.^[10,11] For this reason, surgical resection of metastases continues to play an important role in the management of mRCC and is nowadays an accepted option in carefully selected patients, provided that, if attempted, it is complete.^[1] Due to the presence of multiple abdominal and pulmonary metastases, our patient started treatment with sunitinib. After several years of stable polymetastatic disease with systemic treatment, the progression of retroperitoneal metastases was identified. After complete surgical resection of the metastases progressing under systemic treatment, therapy with sunitinib was resumed, achieving an adequate control of the disease for two additional years.

In conclusion, although more evidence must be obtained with controlled clinical trials at the time of oligoprogression, it is our belief that, in selected patients, iterative metastasectomy can improve prognosis and substantially prolong survival in patients with oligoprogressive mRCC under tyrosine-kinase inhibitors. For this reason, a multidisciplinary approach to patients with mRCC, closely involving medical oncologists and urologists, is of paramount importance to improve survival.

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Conflicts of interest

There are no conflicts of interest.

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