

A case of metastatic renal cell carcinoma treated with sunitinib followed by pulmonary resection

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Introduction

Although relatively rare, kidney cancers, including renal cell carcinoma (RCC), are associated with a poor prognosis^[1]. Until recently, the treatment of metastatic RCC (mRCC) has been limited to immunotherapy with interferon-(IFN)- α and/or interleukin-(IL)-2, although response rates are limited (5–20%)^[2,3]. Growing understanding of RCC pathogenesis has led to a great expansion in the therapeutic options available. Much research has focused on the role of overexpression of growth factors including vascular endothelial growth factor (VEGF) and platelet derived growth factor (PDGF) in tumor angiogenesis and growth^[4]. The introduction of anti-angiogenic therapies targeting these pathways has had an important impact on patient management, resulting in higher response rates and longer progression-free survival than IFN- α ^[4]. Sunitinib is an orally administered inhibitor of multiple receptor tyrosine kinases, including VEGF and PDGF receptors^[5]. It has shown efficacy in treating RCC in clinical trials, with progression-free survival of 11 months and overall survival of 26.4 months and better quality of life than with IFN- α ^[6, 7]. It is currently recommended as first-line therapy and standard of care for advanced or metastatic RCC^[7-9].

Here we report a case study of a patient treated with sunitinib for RCC with lung metastases, resulting in sufficient response to allow surgical resection.

Case report

Patient presentation and history

In September 2007, a 69-year-old man with a history of hypertension was diagnosed with a malignant tumor in the right kidney, which was treated with radical nephrectomy in November 2007. Histological examination of the excised tumor showed that it was a clear cell RCC, staged as pT2N0M0. The patient received no adjuvant therapy, and was followed up regularly, remaining in good health. In February 2010, 29 months after surgery, a CT scan as part of routine follow-up revealed multiple pulmonary nodules (Figure 1a). Histopathological analysis of the biopsy specimen indicated that these were metastases from the original clear cell RCC primary tumor.

Treatment

The patient was treated with sunitinib (50 mg/day) on a 6-week cycle (4 weeks

on followed by 2 weeks off treatment). The treatment was generally clinically and biologically well tolerated with no vomiting, diarrhea or hypertension associated with sunitinib administration.

After three cycles of sunitinib, a chest CT scan showed that only three pulmonary nodules remained in the right upper lobe (Figure 1b). A decision was taken to resect these persisting secondary lung lesions and the patient subsequently underwent a resection of the upper lobe of the right lung. Post-operatively the patient recovered well and remains in good health (October 2011), with no evidence of relapse.

Discussion

Approximately one third of RCC patients present with metastatic disease, and up to 40% treated for localized disease have a recurrence^[10, 11]. Since this tumor type is highly resistant to chemotherapy, the cytokines IL-2 or IFN- α were used for many years as first-line treatment for metastatic disease^[2, 3]. However, low response rates (5–20%) and median overall survival (approximately 12 months) limit the efficacy of these cytokines for RCC treatment.

Better understanding of disease mechanisms and the development of targeted therapies such as sunitinib have expanded the treatment options and improved the prognosis of mRCC. In a Phase III study, sunitinib demonstrated superior efficacy to IFN- α in patients with metastatic RCC who had not received prior systemic therapy^[7]. The progression-free survival with sunitinib was 11 months compared with 5 months with IFN- α and the median overall survival with sunitinib was greater than 2 years^[7]. Furthermore, sunitinib was also associated with a higher objective response rate than was IFN- α (47% vs. 12%, $P < 0.001$)^[7].

In this patient with multiple RCC lung metastases, treatment with sunitinib induced a good response with sufficient shrinkage of the lung metastases to allow surgical resection of the remaining nodules. This case report is in line with accounts in the literature of patients who have achieved long-term survival after resection of metastases persisting after systemic therapy^[12-15]. Targeted therapy alone is rarely curative and when technically feasible, metastasectomy should be considered as part of a multimodal approach to treatment of mRCC. In particular, aggressive surgery can be considered an option in patients with

good prognostic features such as metachronous metastases, a long disease-free interval and a single site of metastatic disease¹⁴.

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Figures

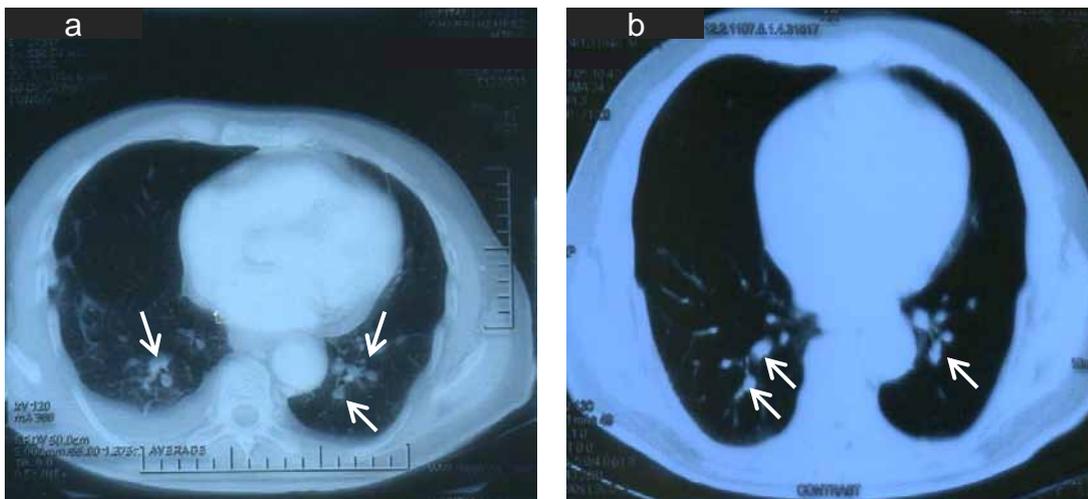


Fig1: (a) Initial CT scan (date) showing metastatic RCC nodules; (b) CT scan following 3 cycles of sunitinib showing tumor response and remaining nodules (marked)