

Neoadjuvant Therapy with Sorafenib in Advanced Renal Cell Carcinoma with Vena cava Extension Submitted to Radical Nephrectomy

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Key Words

Renal cell carcinoma · Nephrectomy · Vena cava thrombus · Multi-targeted tyrosine kinase inhibitor

Abstract

A 71-year-old man with advanced (lymph node involvement and vena cava thrombus) left renal cell carcinoma was submitted to 6 months of neoadjuvant treatment with sorafenib before open radical nephrectomy. After sorafenib treatment and before surgery a new CT scan confirmed the presence of a 9.0 cm in diameter solid mass at the left kidney level but a reduction in thrombus extension, limited to the left renal vein level. At histological examination after radical nephrectomy, over 90% of the renal mass was substituted by necrotic tissue.

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var[®] (Sorafenib) given orally at a dose of 400 mg daily. Treatment with sorafenib was well tolerated without side effects. There was also an improvement in ECOG performance status (score 2), starting after 3 months. In August 2007, a new CT scan confirmed the following: presence of a 9.0 cm in diameter solid mass at the left kidney level (fig. 1b); no modifications at the lymph node level; reduction in thrombus extension, limited at the left renal vein level without involvement of the inferior vena cava (fig. 1d). In September 2007, 6 months after neoadjuvant treatment with sorafenib, the patient was submitted to an open left radical nephrectomy (fig. 2a). No intraoperative or postoperative complications developed.

Pathology

Macroscopic examination at the level of the left kidney showed a 9 × 7 cm solid mass involving the upper pole and the medial aspect of the kidney. The mass was well delimited by a pseudocapsule. The renal capsule, ureter and renal vessels were unaffected by the mass and, in particular, the renal vein was free from thrombus. Histological examination revealed that over 90% of the solid mass was substituted by necrotic tissue: the residual neoplastic component was diagnosed as a clear cell renal cell carcinoma (RCC), Fuhrman grade 2 (fig. 2b). At the pathological examination, all lymph nodes removed were negative for neoplastic involvement.

Clinical Course

Currently (February 2008), the patient is in good physical condition; the ECOG performance status has normalized (score 1), and the quality of life is good. Treatment with sorafenib was interrupted after surgery. At 5 months from radical nephrectomy (February 2008) a new CT scan was negative for local progression or distant metastases. It is important to underline that the patient did not develop embolic events.

Case Report

Presentation and Diagnosis

In March 2007, at CT screening, a 71-year-old white male was diagnosed as having a voluminous (8.0 cm in diameter) solid mass at the left kidney level (fig. 1a). Moreover, the CT scan (chest, abdomen and pelvis) evidenced lymph node involvement (maximal diameter 3 cm, at the para-aortic and left renal vein level) and a thrombus at the level of the left renal vein and inferior vena cava (fig. 1c). No other distant metastases were evidenced (also a bone scan was negative). The ECOG performance status was 3. In March 2007, the patient started a medical treatment with Nexa-

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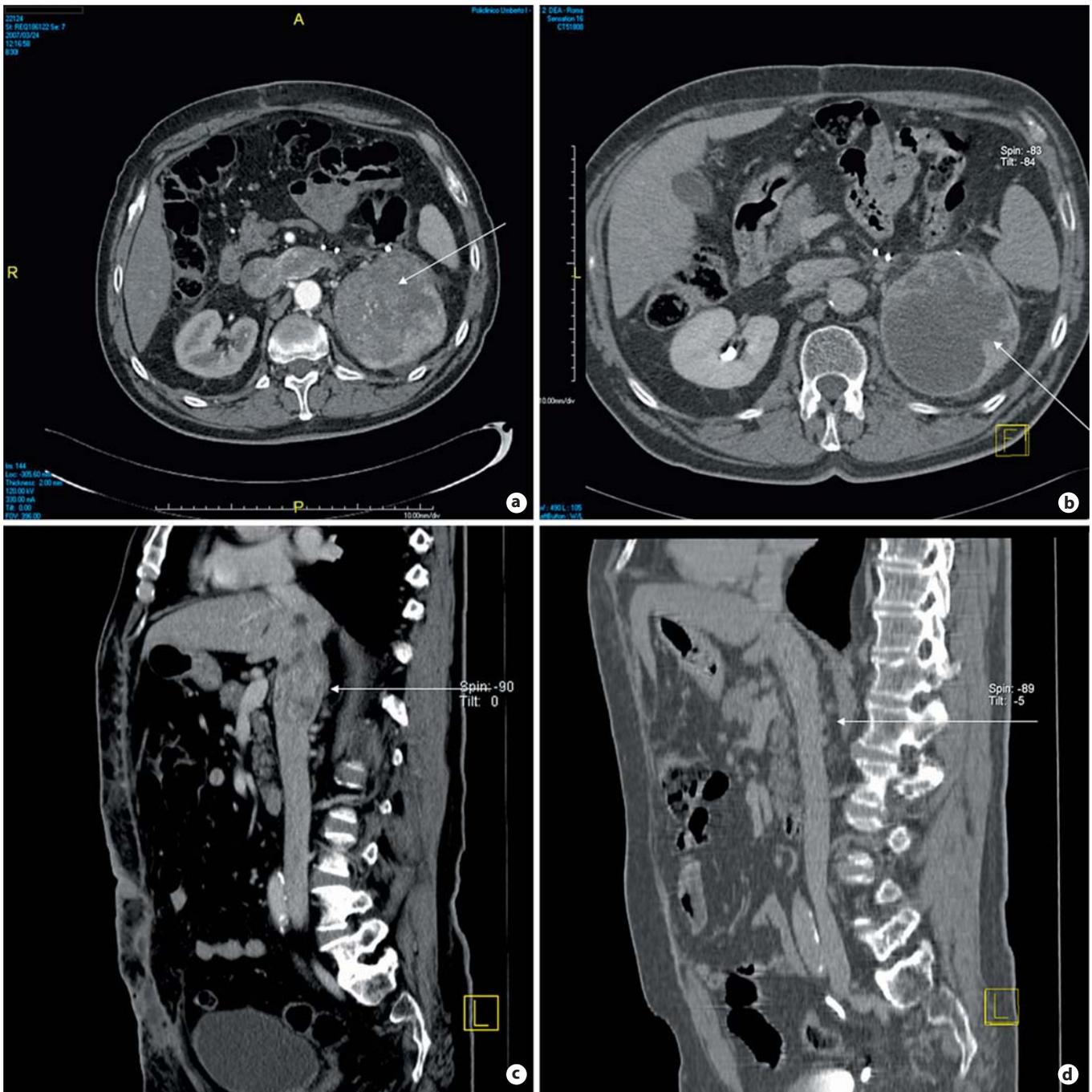


Fig. 1. a Pretreatment (sorafenib) CT scan showing an 8.0-cm left-sided solid renal mass involving the upper pole and the medial aspect of the kidney. **b** Posttreatment (sorafenib) CT scan showing a 9.0-cm left-sided solid renal mass. **c** Pretreatment (sorafenib) CT scan showing a thrombus involving the left renal vein and the inferior vena cava. **d** Posttreatment (sorafenib) CT scan showing a thrombus limited to the left renal vein (no inferior vena cava involvement).

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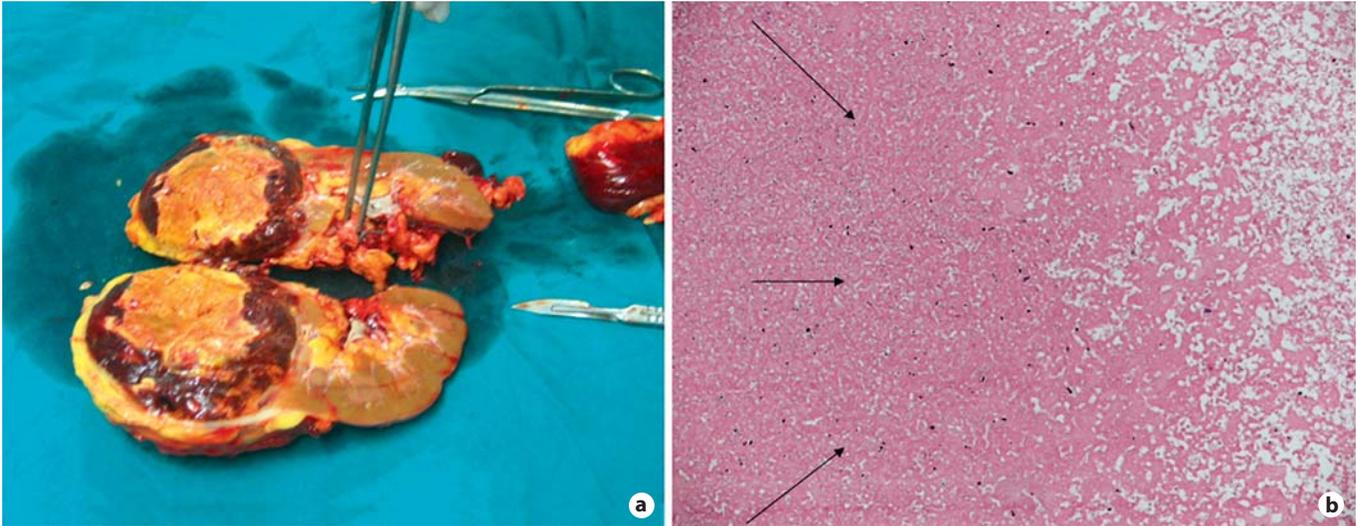


Fig. 2. **a** Left radical nephrectomy. Macroscopic aspect of the 9 × 7 cm solid mass involving the upper pole and the medial aspect of the kidney. **b** Pathological evidence of extensive necrotic tissue (arrows) involving over 90% of renal mass. HE. ×10.

Discussion

In the last years, new advances have begun to revolutionize the management of RCC and offer hope for the future. First, a proven role for aggressive surgical resection of the primary lesion and metastatectomy has been underlined. Second, a series of exciting new approaches, the so called ‘targeted therapy’, are changing the management of advanced RCC [1]. Several studies using strategies to inhibit vascular endothelial growth factor activity have demonstrated significant antitumor effects in the management of RCC [2, 3]. Sorafenib is an oral multikinase inhibitor that targets the vascular endothelial growth factor family and the kinase activity of both C-Raf and B-Raf [4]. Sorafenib was generally analyzed in trials on RCC cases submitted to cytoreductive surgery and in progression after cytokine therapies [5]. The encouraging

results with sorafenib led to trials in all high-risk or metastatic RCC. We report on an extraordinary clinical case of advanced RCC submitted to a 6-month neoadjuvant treatment with sorafenib and radical nephrectomy.

In this way, we also had the opportunity to analyze the effect of sorafenib therapy at the RCC tissue level. We underline three positive results, possibly related to sorafenib neoadjuvant treatment: (1) complete response at the vena cava thrombus level; (2) massive necrotic (over 90%) effect at the left kidney RCC level; (3) positive response at the lymph node level.

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