Complete Histologic Remission after Sunitinib Neoadjuvant Therapy in T3b Renal Cell Carcinoma

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1. Case report

Sunitinib treatment has shown significant improvement in overall survival for metastatic renal cell carcinoma (RCC) [1] as well as in significant metastasis and primary tumour shrinkage [2]. Some recent publications mentioned promising results with neoadjuvant therapy [3,4], inducing partial remission in primary tumour, vena cava thrombus, and lymph node metastases. In this paper, we report the first case of complete histologic remission after sunitinib as neoadjuvant therapy in a T3b RCC.

A 78-yr-old woman with an Eastern Cooperative Oncology Group (ECOG) score of 0 presented with a T3b renal tumour. She refused surgical treatment but agreed to percutaneous biopsy and medical treatment. A Fuhrman III renal cell carcinoma was histologically confirmed on percutaneous biopsy, and sunitinib treatment was administered over 6 mo. A significant objective response was observed for tumour size and thrombus. The patient finally accepted surgical treatment. Pathologic examination concluded with a complete response of primary tumour and thrombus.

The authors present the first case report of complete histologic remission after neoadjuvant sunitinib treatment on primary renal tumour and vena cava thrombus. A 78-yr-old woman with an Eastern Cooperative Oncology Group (ECOG) score of 0 presented with a T3b renal tumour. She refused surgical treatment but agreed to percutaneous biopsy and medical treatment. A Fuhrman III renal cell carcinoma was histologically confirmed on percutaneous biopsy, and sunitinib treatment was administered over 6 mo. A significant objective response was observed for tumour size and thrombus. The patient finally accepted surgical treatment. Pathologic examination concluded with a complete response of primary tumour and thrombus.
department in November 2007 for right-flank pain. Computer tomography (CT) scan and magnetic resonance imaging (MRI) of the abdomen found a 68-mm tumour on the lower pole of the right kidney. Early enhancement of the tumour and extension to the vena cava until the hepatic veins were shown on MRI after injection (Fig. 1). Thoracic CT scan and bone-scan excluded metastatic disease. According to the European Association of Urology (EAU) guidelines, radical nephrectomy and thrombectomy were proposed [5]. The patient refused any kind of surgical treatment but agreed to percutaneous biopsy and medical treatment. Percutaneous biopsy confirmed Fuhrman III renal cell carcinoma (Fig. 2). Starting in December 2007, sunitinib was administered 50 mg daily for 4 wk every 6 wk.

Fig. 1 – Magnetic resonance image of the abdomen at diagnosis: (a) 68-mm tumour of the right kidney and (b) vena cava thrombus extension to the hepatic veins.

Fig. 2 – Microscopic examination of the right kidney tumour percutaneous biopsy: Fuhrman III renal cell carcinoma.

Fig. 3 – Magnetic resonance image of the abdomen after four cycles of sunitinib treatment: (a) 35% regression of the renal tumour and (b) stabilization of the vena cava thrombus.
After two cycles of treatment, 35% regression of the renal tumour and stability of the vena cava thrombus were observed on MRI. Two additive cycles of sunitinib were administered to the patient at a lower dose (37.5 mg daily) due to thrombopenia. Another MRI was performed in July 2008 and showed persistence of partial response in the renal tumour and partial regression of the vena cava thrombus thickness (Fig. 3).

Because of partial imaging response, surgical treatment was finally accepted by the patient. A fifth cycle of sunitinib (37.5 mg daily) was conducted to plan surgery but was interrupted 6 wk before surgery. In October 2008, radical nephrectomy and thrombectomy were performed through an abdominal approach with prior renal artery embolisation. The nephrectomy revealed tight perirenal tissues and adherent vena cava thrombus. No complications were observed during the postoperative period.

Macroscopic examination of the kidney found a lower-pole tumour with evidence of major necrosis (Fig. 4). Pathologic examination confirmed complete tumour necrosis without any sign of malignant cells in the kidney or in the thrombus (Fig. 5). Immunohistochemistry with vimentin, CD10, and AE1/AE3 antibodies was also negative, confirming complete tumour necrosis (Fig. 6). With a 3-mo follow-up, no evidence of local or metastatic disease was found.

2. Discussion

This case illustrates the potential of neoadjuvant antiangiogenic therapy in the surgical management of RCC.

Sunitinib treatment has been widely studied in metastatic RCC as a complement to radical nephrectomy. It has achieved progression-free and overall survival improvement more than other treatments.
It is currently considered to be the new reference standard for first-line treatment in metastatic RCC. It has proven efficacy for metastasis regression as well as for primary tumour size reduction.

We are reporting the first case of complete histologic remission after neoadjuvant sunitinib treatment. The patient had locally advanced RCC with important extension to the vena cava, and surgical treatment was difficult. Neoadjuvant therapy reduced surgical risks to make treatment acceptable to the patient.

Other recent publications are reporting interesting effects of sunitinib as neoadjuvant therapy. Shuch et al. have shown a significant response after neoadjuvant sunitinib treatment for three patients. These patients were contraindicated for surgical treatment because of large tumour size on a solitary kidney, atrial thrombus, or major lymph node metastasis. All were accessible to surgical treatment after neoadjuvant treatment, thanks to the reduction of primary tumour, vena cava thrombus, and lymph node metastasis. Amin et al. confirmed these effects of neoadjuvant sunitinib and sorafenib on nine patients with locally advanced or metastatic RCC. Tumour reductions were observed on the primary tumour as well as in the metastatic sites. Neoadjuvant treatment permitted radical nephrectomy. Karakiewicz et al. described one case of T3b sunitinib neoadjuvant therapy. In this patient, renal tumour decreased from 11 cm to 8 cm and thrombus downstaged from atria to the renal vein.

From these observations, we assume that antiangiogenic treatments could change strategies of care for locally advanced or metastatic RCC. It could allow surgical treatment in some contraindicated patients or reduce surgical risks. The role of antiangiogenic agents as neoadjuvant therapy should be further studied in randomised trials.

Conflicts of interest: A. Ravaud is a member of the global, European, and/or French boards of Pfizer, Bayer, Schering, Novartis, Roche, GSK and Wyeth for urologic tumours, and he receives institutional support for research from Roche, GSK, and Novartis. G. Robert, G. Gabbay, R. Bram, H. Wallerand, C. Deminière, F. Cornelis, JC. Bernhard, and P. Ballanger have nothing to disclose.

EU-ACME question

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Question:

According to the European Association of Urology guidelines, what is the correct indication for sunitinib treatment in renal cell carcinoma (RCC)?

A. Neoadjuvant therapy in locally advanced RCC.
B. Neoadjuvant therapy in metastatic RCC.
C. First-line treatment before radical nephrectomy in metastatic RCC.
D. First-line treatment after radical nephrectomy in metastatic RCC.

References