Case Report
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Impact of Neoadjuvant Sunitinib Treatment on Tumour Thrombi in the Inferior Vena Cava in Metastatic Renal Cell Carcinoma

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Abstract

The authors report cases of metastatic renal cell carcinoma with level III-IV tumour thrombi in the inferior vena cava (IVC). Cases were treated with three courses of neoadjuvant sunitinib to reduce the thrombus level before surgery.
Nephrectomy and tumour thrombectomy were performed, and sunitinib treatment continued after the operation.
Cases 1 and 3 showed regression of lung metastases, but the size of the primary renal tumour and thrombus remained the same. The progression-free survival of the cases was 35 months and 24 months, respectively. In case 2, the primary renal tumour, metastases and thrombus showed regression. The upper limit of the thrombus decreased by 3 cm. In this case, the progression-free survival was 15 months, and the cancer-specific survival was 18 months.
The neoadjuvant sunitinib treatment had a limited effect on downsizing the extent of tumour thrombi in the IVC.
Keywords: Inferior vena cava, neoadjuvant sunitinib, metastatic renal cancer, radical nephrectomy, tumour thrombus

Introduction

Progression of renal cancers into the inferior vena cava (IVC) is relatively rare and is sometimes associated with presence of distant metastases. The conventional treatment for metastatic renal cancer with a tumour thrombus in the IVC is radical nephrectomy with concomitant tumour thrombectomy, followed by targeted molecular therapy. Currently, there are relatively limited publicised data on the impact of neoadjuvant sunitinib therapy on tumour thrombi in the IVC (1,2,3,4,5).

Case Presentation

We report a series of patients who received neoadjuvant sunitinib treatment for metastatic renal cell carcinoma with a tumour thrombus in IVC. Tumour thrombus levels were determined according to Novick's classification. The tumours were in the intermediate risk group based on Memorial Sloan Kettering Cancer Center criteria. Patients received three courses of neoadjuvant sunitinib treatment, 50 mg/day for 4 weeks followed by a 2-week break before surgery. Afterward sunitinib treatment, the patients underwent abdominal and chest computed tomography (CT) exams and were evaluated according to the response evaluation criteria in solid tumours (RECIST) 1.1 criteria.

Case 1

A 66 year old male patient had macroscopic haematuria and an abdominal ultrasound described an 8 cm tumour in the left kidney. Abdominal and chest CT exams showed a suprahepatic tumour thrombus in the IVC (level IV), multiple lung metastases and metastases in the left adrenal gland. Renal biopsy revealed clear cell renal carcinoma. After neoadjuvant sunitinib treatment, the CT control showed a regression of lung metastases, but the size of the primary renal tumour did not change. The upper level of the tumour thrombus also did not decrease (Figure 1) (Table 1).

Radical nephrectomy and tumour thrombectomy were performed and histologic analysis revealed grade 2 clear cell carcinoma with pT3c, pN0, pM1 stage.

After the surgery, sunitinib therapy was continued according to the protocol with follow-up CT exams performed every two cycles. The actual progression-free survival (PFS) of the patient was 35 months.

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Case 2

A 50 year old female had a deep vein thrombosis and a routine abdominal ultrasound discovered a 14 cm tumour in the right kidney. The CT exam revealed a renal tumour with a tumour thrombus extending into the right atrium (level IV), as well as multiple liver and retroperitoneal lymph node metastases. Renal biopsy revealed clear cell renal carcinoma. After neoadjuvant sunitinib treatment, the follow-up CT showed partial regression of both the renal tumour and liver metastases. The upper limit of the thrombus decreased by 3 cm, but it remained a level IV thrombus (Figure 2). Radical nephrectomy was performed, but tumour thrombectomy was unsuccessful. Histology of the resected tumour revealed grade 2 clear cell renal carcinoma with pT3a, pN0 stage. Following radical nephrectomy, sunitinib treatment was continued according to the protocol. Fifteen months after the radical nephrectomy, the control CT demonstrated a new liver metastasis, and sunitinib therapy was ceased. The patient's PFS was 15 months and the cancer-specific survival was 18 months.

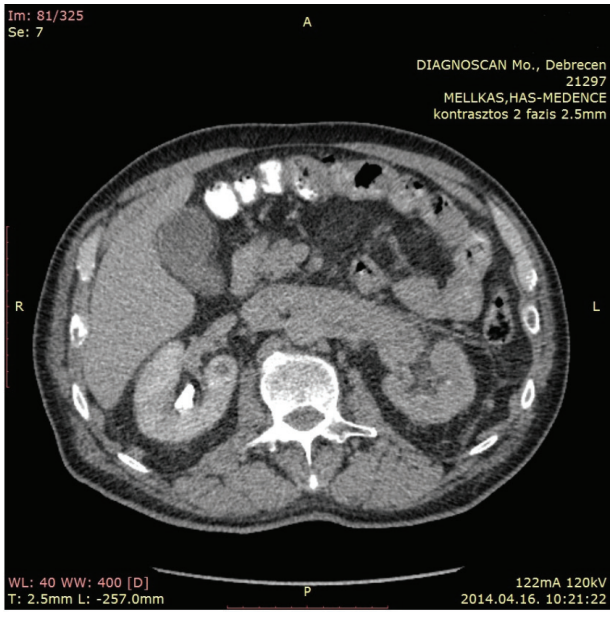

Figure 1. Abdominal computed tomography after the neoadjuvant sunitinib treatment in Case 1 (axial section)

Table 1. Control computed tomography findings after the neoadjuvant sunitinib treatment	
Case 1	**Tumour response**
Renal tumour	Stable
Lung metastases	Regression
Tumour thrombus	No change
Case 2	
Renal tumour	Regression
Liver metastases	Regression
Tumour thrombus	Decreased by 3 cm
Case 3	
Renal tumour	Stable (but necrosis)
Lung metastases	Regression
Tumour thrombus	No change

Case 3

A 52 year old male patient had a visible mass protruding from the upper right abdomen. Ultrasound showed a 22 cm tumour in the right kidney. Chest and abdominal CT exams showed a renal tumour with multiple lung and retroperitoneal lymph node metastases, as well as an intrahepatic tumour thrombus in the IVC (level III). Renal biopsy revealed clear cell carcinoma. After neoadjuvant sunitinib therapy the follow-up CT showed partial regression of lung metastases. The CT did not show changes in the bulk size of the renal tumour or the thrombus (Figure 3). Surgery was performed and the histology revealed grade 2 clear cell carcinoma with pT3c, pN2 stage. After the operation, sunitinib therapy was continued according to the protocol. CT

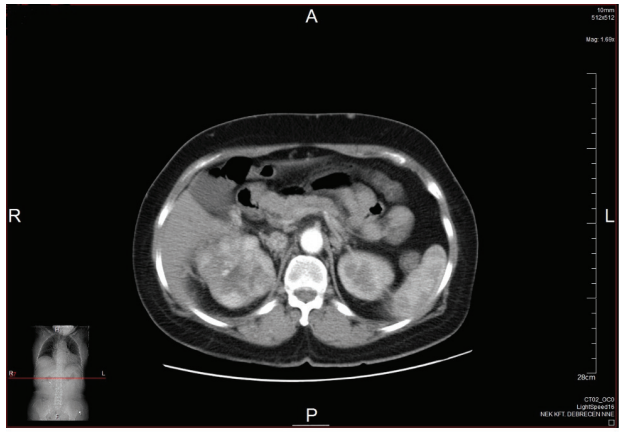

Figure 2. Abdominal computed tomography after the neoadjuvant sunitinib treatment in Case 2 (axial section)

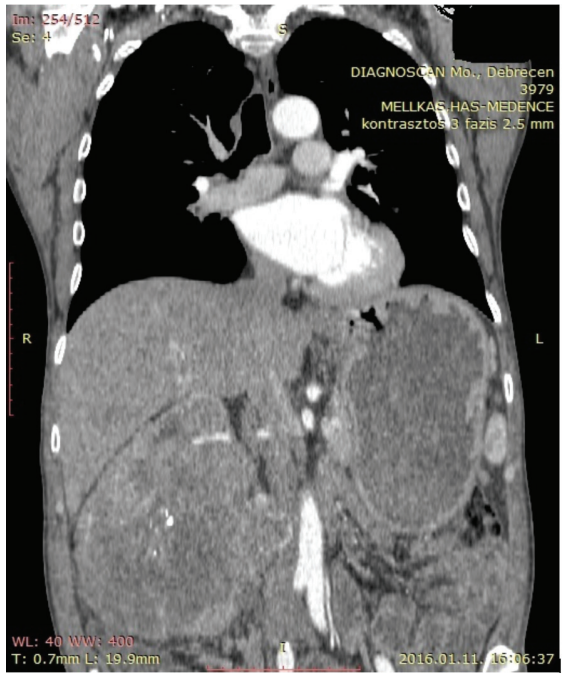

Figure 3. Abdominal computed tomography after the neoadjuvant sunitinib treatment in Case 3 (coronarial section)

control follow-up exams showed a stable disease on RECIST 1.1, with a PFS of 24 months.

Discussion

Surgery of renal tumours with IVC thrombi has a relatively high complication rate, ranging from 12% to 46%. Several physicians have tried to reduce the size of tumour thrombi with administration of neoadjuvant targeted molecular therapy to decrease the rate of complications.

Current literature only provides a few publications in which neoadjuvant therapy has been used to downsize tumour thrombi in the IVC. Generally in these patients, two to four cycles of the targeted therapy were administered before the operation. Of the limited publications, the majority consist of case reports. Some authors described regression of tumour thrombi after neoadjuvant sunitinib therapy in their individual cases (6,7,8). Karakiewicz et al. (7) were the first to report a significant decrease of the thrombus level in the IVC (from level IV to level II) after sunitinib therapy, facilitating easier surgical procedure. Peters et al. (8) described a case in which there was a significant reduction in primary tumour size and metastatic sites, and the IVC thrombus downstaged from level IV to level III according to Novick classification as a result of preoperative sunitinib treatment.

However, in contrast to the mentioned cases, other reports have showed that neoadjuvant therapy was not always successful at downstaging the IVC thrombus level, and progression of the thrombus level was observed (3,9).

Cost et al. (3) studied the efficacy of targeted molecular therapy at decreasing the level of renal cell carcinoma vena cava tumour thrombi in 24 patients. Their data showed that the thrombus level remained unchanged in 21 patients (84%), decreased in three patients (12%) and increased in one patient (4%) during the treatment. Of the three cases that showed thrombus regression, only one case had enough of an impact to affect the surgical procedure (level IV to III). During the study, the size of the primary tumour increased in 10 patients (40%), decreased in 12 (48%), and did not show any change in three (12%) cases.

Bigot et al. (1) performed a retrospective analysis of 14 patients with renal cell carcinoma with IVC thrombus treated with neoadjuvant sunitinib therapy before the surgery. In the study, six (43%) patients had a measurable decrease in thrombus size, six (43%) had no change, and two (14%) had an increase. In regard to the thrombus size, 12 patients (85%) had stable thrombus, one patient (7%) had a downstage of thrombus level, and one patient (7%) had an upstage of thrombus level. In the one patient who demonstrated a downstaging of the thrombus (level II to level I), the downstaging was not significant enough to affect the surgical intervention. Follow-up CT exams after the neoadjuvant sunitinib treatment showed that the primary renal tumour remained stable in five patients (36%), showed regression in seven patients (50%), and showed progression in two patients (14%) (1).

In our cases, regression of the tumour thrombus was detected in only one case, but the tumour thrombus level in that case remained the same (level IV). Neoadjuvant treatment resulted in regression of the distant metastases in all cases, but the size of the primary tumour decreased in only one patient.

Conclusion

Effective downstaging of the tumour thrombus in the IVC was not achieved in our cases with neoadjuvant sunitinib treatment. Although sunitinib treatment had noticeable effects on primary tumour size, metastases and survival, it had a limited effect on downsizing the extent of tumour thrombus in the IVC and did not affect the overall surgical outcome in this regard.

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Ethics

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Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Supervision: T.S., Concept: C.B., Design: T.F., C.B., Data Collection or Processing: A.B., Analysis or Interpretation: T.S., Literature Search: B.J., Writing: A.B., T.F., B.J.

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