Case Study of the Month

Neoadjuvant Sutent Induction Therapy May Effectively Down-Stage Renal Cell Carcinoma Atrial Thrombi

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Abstract

A 75-yr-old previously healthy woman presented with gross hematuria, European Cooperative Oncology Group 0, and an 11-cm renal mass with right atrial thrombus. The patient refused the sternotomy. She was offered two cycles of sunitinib maleate (Sutent) induction therapy to down-stage the thrombus and to reduce the extent of the surgery.

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1. Case report

A 75-yr-old previously healthy woman presented with gross hematuria and European Cooperative Oncology Group 0 performance status. The physical examination was unremarkable. An abdominopelvic computed tomography (CT) scan demonstrated an 11-cm left renal mass with central necrosis, which appeared confined within Gerota’s fascia. The renal vein was dilated and contained a tumor thrombus (Fig. 1). It filled the entire circumference of the vein and the inferior vena cava (IVC). Venous collateral circulation and dilated retroperitoneal and pelvic veins were reported. There were no radiographically visible nodal metastases. Chest and brain CT scans ruled out distant metastases. Cardiac echography showed a 1 × 2-cm intra-atrial thrombus (Fig. 2). Nephrectomy and thrombectomy were offered as primary treatment options. However, the patient refused the sternotomy for fear of complications related to cardiac bypass and possible need for cardiac arrest. The option of neoadjuvant thrombus cytoreduction with sunitinib maleate (Sutent) was offered. Empirically, two cycles of therapy were administered, without grade 3 or 4 toxicity, to downstage the thrombus and to obviate the need for a sternotomy. Twelve weeks after initiation of sunitinib therapy, magnetic resonance imaging (MRI) showed a decrease in the maximal tumor dimension from 11 to 8 cm. The tumor thrombus (Fig. 3) was...
down-staged to a small tissue mass on a thin stalk, which barely protruded beyond the ostium of the renal vein. Two weeks later, the surgical specimen confirmed the significant down-staging of the tumor thrombus (Fig. 4).

2. Discussion

Renal cell carcinoma (RCC) may invade the rein vein and eventually extend all the way up the IVC and into to the right atrium. Up to 10% of patients present with IVC invasion [1]. Substantially fewer present with right atrium thrombus extension (level IV). RCC with renal vein or IVC extension is rare and few series describe the surgical and cancer control outcomes of such patients [1–4]. Glazer and Novick
described the long-term survival of 18 patients with atrial thrombi [5]. As long as the primary tumor remained localized to the kidney, the cephalad IVC or atrial extension was consistent with long-term survival. Overall 5-yr survival with atrial thrombus extension was 56.6% and cancer-specific survival was 60.2%. Without renal capsular penetration, the mean survival was 58 mo versus 19.7 mo in the presence of perinephric fat invasion. Recently, Haferkamp et al [1] demonstrated the prognostic significance of the level of thrombus extension and its independent predictor status (hazard ratio 1.8, \( p = 0.03 \)). Patients with level I or II thrombi had a survival of 25 mo survival versus 13 mo for patients with level III or IV thrombi. The authors [1] demonstrated dismal survival for 23 nonsurgically treated patients (6.9 mo) versus 19.8 mo for 111 surgical patients. The 30-d operative mortality rate was 10% versus 13% mortality at 30 d in the nonsurgical cohort. Taken together these data demonstrate that long-term survival is possible in patients with cephalad extension of IVC thrombus as long as the tumor is localized to the kidney and surgically resected. However, perioperative mortality is not negligible and emphasizes the high risk of nephrectomy and thrombectomy cases. The challenge is particularly important for those with thrombus extension well above the diaphragm. For level III (up to the atrium) and IV (atrial) thrombi, the surgery requires a triradiate incision, with the added morbidity from its sternotomy aspect. Complete liver mobilization and circumferential mobilization of the IVC are required. Moreover, the diaphragm and the pericardium need to be opened to allow intrapericardial IVC mobilization. Subsequently, the thrombus may be reduced to the infradiaphragmatic and ideally to the infrahepatic part of the IVC, to facilitate its complete removal. Cardiopulmonary bypass with or without cardiac arrest might be required for atrial extension (level IV). Relative to an abdominal approach a sternotomy and its associated additional surgical maneuvers represent sources of added morbidity, which may discourage some patients from a surgical intervention [1].

Based on the added risk of treating level III and IV thrombi, it could be argued that down-staging of level III or IV tumor thrombi to level IIIa or lower could reduce surgical morbidity and mortality. Data from phase 2 and 3 trials of kinase inhibitors demonstrated a down-staging effect of these agents, when tumor burden was examined radiographically [6–8]. However, the effect of either of the kinase inhibitors has not been reported in patients with tumor thrombi. Despite the absence of such data, we decided to offer this option to this otherwise healthy 75-year-old woman. Our clinical observations confirmed the powerful cytoreductive effect of sunitinib, which down-staged the tumor thrombus from the right atrium to the infrahepatic portion of the IVC, where the thrombus became accessible through an exclusively abdominal approach. Our findings indicate that sunitinib offers cytoreductive possibilities, which may entirely change the existing surgical paradigms related to the management of locally advanced RCC. Use of these agents may allow us to surgically remove the disease with less morbidity and reduced mortality. However, caution is needed when the potential cytoreductive benefits of sunitinib are considered. Down-staging may be associated with treatment toxicity and may not translate into better survival. Only prospective randomized trials addressing the neoadjuvant down-staging effects of kinase inhibitors will prove or disprove the enthusiasm of this preliminary report. Nonetheless, our data indicate that sunitinib offers a tremendous potential for down-staging of locally advanced RCC and may offer a better chance for safe and effective surgical cancer control.

**Conflicts of interest**

The authors have nothing to disclose.

**EU-ACME question**

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**Question:**

What are the treatment options for patients with renal cell carcinoma and inferior vena cava thrombus?

A. Nephrectomy and thrombectomy
B. Embolization
C. Cytoreductive kinase inhibitor therapy followed by nephrectomy and thrombectomy
D. All of the above

**References**


