Renal Tumor with Thrombus in the Inferior Vena Cava and Vertebral Metastases

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Abstract

Introduction and Objectives. The renal cell carcinoma with inferior vena cava (IVC) thrombus extension occurs in 4-10% of cases. Reported mortality rates for radical nephrectomy with concomitant IVC thrombectomy range between 5-12%. The association of bone metastases adds to the difficulty in choosing the best therapeutic option.

Materials and Methods. We present the case of a female patient M.L., 43 years of age, who presented for right persistent intercostal neuralgia and was investigated for a dorsal vertebral mass (T9) in a Neurosurgical Department. A T9 laminectomy and the ablation of a right epidural paramedian tumor were performed. The pathological examination confirmed the suspicion of bone metastasis, of probable renal origin. This was further demonstrated by magnetic resonance imaging (MRI), that revealed a right renal tumor T3bNxM1 (space-occupying lesion, measuring 75/52/72 mm, in the lower half of the right kidney, extended into the renal vein and for 24 mm into the IVC). Through a thoraco-abdominal approach, a right nephrectomy and IVC thrombectomy were performed.

Results. The pathological examination showed a renal cell carcinoma (clear cell with acidofilic cell predominence), Fuhrman grade 3. The early postoperative period was uneventful for 2 weeks after the nephrectomy, but the sudden onset of dorsal vertebral pain associated with paraparesis, required the emergency admission in the Neurosurgical Department. The ablation of a dorsal spinal mass was performed, along with vertebral fixation with a bilateral T7-T11 pedicular system. Afterwards, the complex treatment of the case included the initiation of the biological therapy with angiogenesis inhibitors (Sunitinib).

Conclusions. The selection of cases for radical nephrectomy and IVC thrombectomy should be limited to patients with an anticipated good performance status. Even if the presence of bone metastases has an adverse effect on the survival, the oncological progress in the targeted molecular therapies is an argument for the above-mentioned approach.

Key-words: renal cell carcinoma, venous tumor thrombus, metastasis, cytoreductive nephrectomy, targeted molecular therapy.

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Introduction and Objectives

Renal cell carcinoma (RCC) accounts for approximately 3% of adult malignancies. About 25% of patients with RCC have metastatic disease at presentation and up to 10% of these cases have tumor thrombus into the IVC [1].

The emerging of targeted therapy offers more choices for metastatic renal cell carcinoma (mRCC) and has prompted a reevaluation of cytoreductive surgery. Cytoreductive neprectomy is defined as the surgical removal of the primary RCC lesion before initiation of systemic therapy. Although CN with IVC thrombectomy is performed with acceptable complication rates, it remains unclear whether surgery is still a good choice for concomitant mRCC with IVC tumor thrombus.

Thus, we have reviewed the literature evaluating the benefits (clinical and oncological) of CN with thrombectomy before targeted molecular therapy (TMT) in these patients and the primary end point analyzed was the overall survival (OS).

Materials and Methods

A 43 year-old female patient M.L. was admitted in a Neurosurgical Department for right persistent intercostal neuralgia and was investigated for a dorsal vertebral mass (T9).

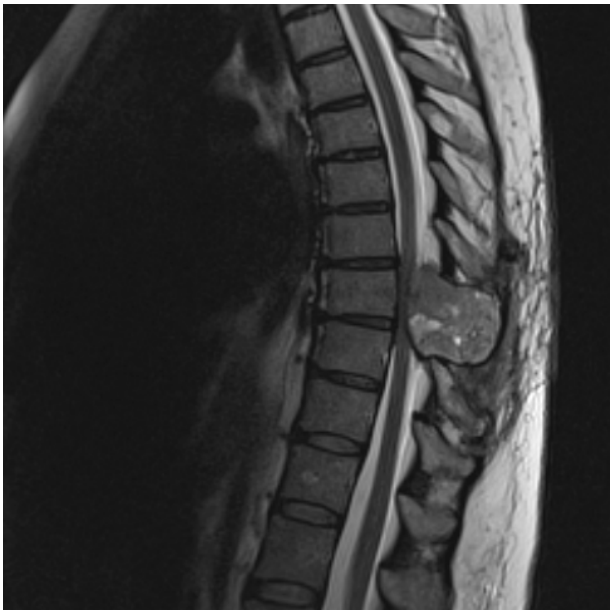


Figure 1 Dorsal vertebral mass T9 (MRI)

A T9 laminectomy and the ablation of a right epidural paramedian tumor were performed. The pathological examination confirmed the suspicion of bone metastasis, of probable renal origin. This was further demonstrated by magnetic resonance imaging (MRI), that revealed a right renal tumor T3bNxM1 (space-occupying lesion, measuring 75/52/72 mm, in the lower half of the right kidney, extended into the renal vein and for 24 mm into the IVC).



Figure 2 Right renal tumor (MRI)



Figure 3 IVC thrombus in coronal plane (MRI)

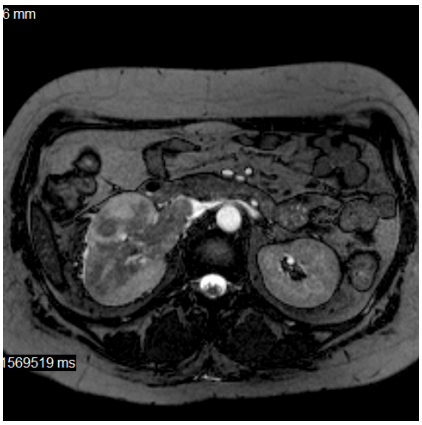


Figure 4 IVC thrombus in axial plane (MRI)

Through a thoraco-abdominal approach, a right nephrectomy and IVC thrombectomy were performed. After early ligation of the right renal artery, in the space between the IVC and the aorta, the anterior and lateral surface of IVC was exposed. Vascular clamps were placed on the contralateral renal vein and on the IVC, below and above the thrombus. After cavotomy, the thrombectomy was performed safely. Then, the right nephrectomy was completed and closure of cavotomy was done with 4-0 Prolene running suture.

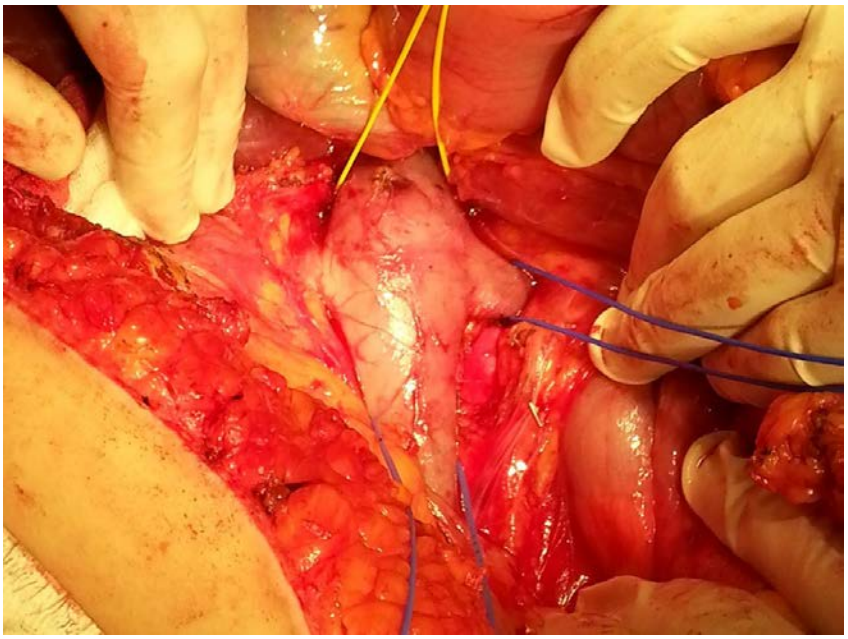


Figure 5 Dissection of IVC and left renal vein

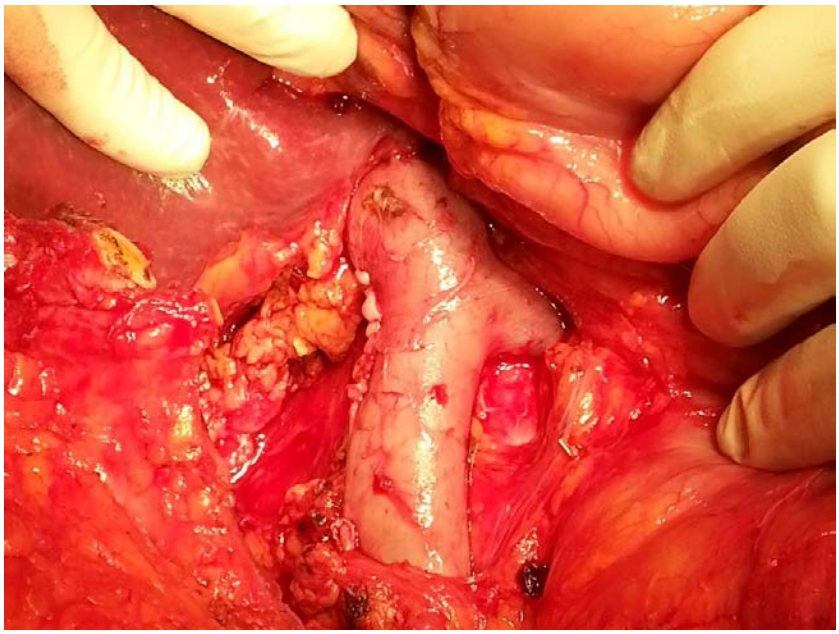


Figure 6 Aspect following right nephrectomy and cavoraphy

Results

The pathological examination showed a renal cell carcinoma (clear cell with acidofilic cell predominence), Fuhrman grade 3. The early postoperative period was uneventful for 2 weeks after the nephrectomy, but the sudden onset of dorsal vertebral pain, associated with paraparesis, required the emergency admission in the Neurosurgical Department. The ablation of a dorsal spinal mass was performed, along with vertebral fixation with a bilateral T7-T11 pedicular system. Afterwards, the complex treatment of the case included the initiation of the biological therapy with angiogenesis inhibitor (Sunitinib). The subsequent oncologic follow-up showed slow bone metastasis tumor progression, the patient being alive 3 years after the surgical procedure.

Discussions

The natural history of untreated RCC with venous tumor thrombus is poor, with a median survival of 5 months and a 1-year disease-specific survival (DSS) of only 29%. In patients presenting with metastatic disease, 1-year DSS is 23% (median DSS: 4 months) for those with thrombus below the diaphragm and 10% (median DSS: 3 months) for those with thrombus above the diaphragm [2]. For those with distant metastases at the time of diagnosis who underwent surgery, 1-year survival is 60% and this finding highlights the importance of surgery on their prognosis [3].

Radical nephrectomy with IVC thrombectomy is a difficult and potentially complicated procedure with significant risk of morbidity and mortality. Careful preoperative planning is essential to optimizing the outcomes within this patient cohort. High quality and detailed preoperative imaging studies help delineate the proximal extension of the IVC tumour thrombus and possible caval wall direct invasion while determining the potential necessity for intraoperative vascular bypass.

Aggressive surgical resection of the primary renal tumor and caval thrombus is the mainstay of therapy for patients with RCC invading the vena cava who do not have metastatic disease. Overall, radical nephrectomy with concomitant IVC thrombectomy has been shown to have a reported perioperative mortality rate of 5 – 10% [4] and is associated with significant morbidity, with a 38% overall complication rate [5]. Also, the 5-year overall survival remains only between 32% and 69%, highlighting the adverse prognosis of such locally advanced tumours [6]. However, in patients with metastatic disease who undergo resection of the primary tumor and a caval thrombus, survival rates have been less than 15% 5 years after surgery [7].

Tumour resection is curative only if all tumour deposits are excised. For most patients with metastatic disease, CN (cytoreductive nephrectomy) is palliative and systemic treatments are necessary [8].

Retrospective studies suggest that mRCC patients with IVC tumor thrombus may experience improved survival after surgical resection and systemic therapy. Compared with surgery alone and targeted therapy alone, cytoreductive surgery before targeted therapy improved the overall survival and cancer-specific survival of mRCC with venous tumor thrombus [3]. There may be also a palliative benefit to nephrectomy and IVC thrombectomy, particularly if the patient has local symptoms (i.e. intractable haematuria, abdominal/flank pain, and/or shortness of breath) [7].

Although 30-50% of RCC patients with venous thrombus have metastatic disease at presentation, there are minimal data evaluating prognostic factors for OS following CN in patients with tumor thrombus. Case selection is important to identify mRCC patients who are most likely to benefit from cytoreductive nephrectomy (CN). Recent studies have suggested that mRCC patients who are identified as poor risk according to specific criteria should not be selected for surgery since survival is similar with systemic treatment alone [9,10].

Despite better systemic therapies, the median OS for mRCC patients remains less than 2 years [11]. Multi-institutional data demonstrates a benefit for CN in patients treated with targeted therapies, but it is clear that patient selection is important, with non-surgical treatment recommended for patients with expected survival less than 8-12 months. Although upfront surgery is potentially beneficial for many mRCC patients with tumor thrombus to prevent morbidity or death associated with thrombus progression, surgery is unlikely to provide significant benefits for mRCC patients with a high risk of early mortality, since life expectancy can be limited.

No differences of the OS were identified in patients regarding the age, body mass index, race, gender, presence of local symptoms, number of metastatic sites, or location of metastatic sites. Patients with early mortality were more likely to have raised serum LDH, level of thrombus above the diaphragm, high nuclear grade, systemic symptoms (anorexia, fatigue, fever, weight loss > 5 kg, or malaise) or preoperative identification of sarcomatoid features by renal biopsies [12].

The era of targeted treatment needs prognostic models and updated survival data for accurate clinical trial design, patient counselling, and risk-specific treatment. The most widely used system is the Memorial Sloan-Kettering Cancer Center (MSKCC) model, which contains 5 features associated with a shorter survival: low Karnofsky performance status (<80%), high serum lactate dehydrogenase, low hemoglobin, high serum calcium (>10 mg/dL), and absence of prior nephrectomy. These were used as risk factors to categorize patients into three different groups. The median time to death in the 25% of patients with zero risk factors (favorable-risk) was 20 months. 53% of the patients had one or two risk factors (intermediate-risk), and the median survival time in this group was 10 months. Patients with three or more risk factors (poor-risk), who comprised 22% of the patients, had a median survival time of 4 months [13].

The International Metastatic RCC Database Consortium (IMDB) identified 6 independent predictors of poor survival: Karnofsky performance status of less than 80%, less than 1 year from diagnosis to treatment, anaemia, hypercalcaemia, neutrophilia and thrombocytosis. Patients were classified into a favorable-prognosis group (with 0 poor prognostic factors), intermediate-prognosis group (with 1–2 poor prognostic factors) and poor-prognosis group (with 3–6 poor prognostic factors). The favorable-, intermediate-, and poor-prognosis groups accounted for 23, 51 and 26% of all patients. [11].

These two prognostic models have demonstrated the ability to predict early mortality in mRCC patients. In addition to prognostic factors from the risk models, early mortality was more likely in patients with systemic symptoms, patients with level 4 thrombus and patients with sarcomatoid features in their primary tumor [9]. Upfront CN should not be standard management in poor MSKCC/IMDC-risk patients or in cases with other poor prognostic features.

Conclusions

Compared with cytoreductive surgery alone and targeted therapy alone, CN with thrombectomy before targeted therapy may offer better survival for mRCC patients with venous tumor thrombus.

Surgery for mRCC patients with tumor thrombus is complex and may not be beneficial for some patients with very poor OS. Careful selection is critical to identify mRCC patients who are most likely to benefit from CN.

The decision for cytoreductive surgery in mRCC patients with tumor thrombus should be considered on a case by case basis, after consultation with multidisciplinary team including urology, medical oncology, anesthesiology, and other surgical specialties (thoracic surgery or hepatobiliary surgery).

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