

Oncology

Level IV tumor thrombus in non-metastatic renal cell cancer? No, thanks. Level II is better. Lessons learned from a case report

Andrea Benedetto Galosi^a, Alessio Papaveri^a, Daniele Castellani^{a,*}, Edoardo Agostini^a, Luciano Burattini^b, Lucio Dell'Atti^a

^a Department of Specialist Clinical Science and Odontostomatology, Urology Division, Università Politecnica delle Marche, Via conca 71, 60126, Ancona, Italy

^b Department of Molecular and Clinical Science, Medical Oncology Division, Università Politecnica delle Marche, Via conca 71, 60126, Ancona, Italy



ARTICLE INFO

Keywords:

Kidney neoplasms
Pazopanib
Cavoatrial tumor thrombus
Targeted molecular therapies

ABSTRACT

Up to 19% of patients with renal cell carcinoma present with a venous thrombus at diagnosis and 1% have a thrombus extending above the diaphragm. The higher the thrombus level, the more challenging the surgery. Cavoatrial tumor thrombus usually requires circulatory arrest and sometimes cardiopulmonary by-pass. We present a case of non-metastatic renal cell carcinoma with a cavoatrial tumor thrombus in a patient who was unfit for cardiac surgery. Eight months of targeted molecular therapy downsized the tumor thrombus to inferior vena cava and allowed us to perform a radical nephrectomy with minimal cavotomy for thrombus resection.

Introduction

Up to 19% of patients with renal cell carcinoma (RCC) present with a venous thrombus and 1% have a thrombus extending above the diaphragm.¹ Thrombus venal extension is classified according to the Mayo Clinic classification, from level 0 (limited to the renal vein) to level IV (atrial involvement).¹ The higher the thrombus level, the more challenging the surgery. Level IV thrombus requires the involvement of a cardiothoracic surgeon, and circulatory arrest is usually essential for atrial thrombectomy in most cases.² Significant and greater perioperative complications increase with the extent of the tumor thrombus.¹ We report a case of the cytoreductive effect of targeted molecular therapy on a level IV tumor thrombus in an elderly patient with non-metastatic RCC and the subsequent treatment.

Case presentation

A 79-year old lady was referred for a right kidney tumor found incidentally during an abdominal ultrasound performed for abdominal tenderness. Whole-body contrast-enhanced computed tomography (CT) scan confirmed a right kidney tumor measuring 5 cm × 6 cm (Fig. 1A) with a level IV thrombus (Fig. 1B). CT scan showed no lymphatic neither visceral and bone metastasis. Transesophageal echocardiography

confirmed the intra-atrial localization of the thrombus. She had a history of chronic kidney disease, hypertension, and type II diabetes. Her body mass index was 30 kg/m². The cardiothoracic surgeon deemed her unfit for atrial thrombectomy with cardiopulmonary bypass and deep hypothermic circulatory arrest. Then, the patient underwent a renal biopsy. The specimen was diagnostic for clear cell RCC. She started therapy with pazopanib 400 mg daily. The treatment was well tolerated. Eight months later, a contrast-enhanced CT scan showed a minimal shrinkage of the renal tumor (Fig. 2A), and a reduction in extension of the thrombus, located in the inferior vena cava at 5 cm below diaphragmatic hiatus (Level II) (Fig. 2B). After two weeks of drop-out, the patients underwent right radical nephrectomy, with extended retroperitoneal lymph node dissection and small cavotomy through a midline laparotomy (Fig. 3A). The tumor thrombus was free-floating into the vena cava wall and it was completely removed with the aid of a milking maneuver (Fig. 3B). Blood loss was 200 ml. The postoperative stay was uneventful and the patient was discharged 7 days after surgery. Pathology showed a clear cell renal cancer, nuclear grade 2, with regressive aspects and coagulative and necrotic areas (pT3b N0). At 7-month follow-up the patient was disease-free.

* Corresponding author. Department of Specialist Clinical Science, Urology Division, Università Politecnica delle Marche, Via conca 71, 60126, Ancona, Italy.

E-mail addresses: a.b.galosi@univpm.it (A.B. Galosi), alessio.papaveri@gmail.com (A. Papaveri), castellanidaniele@gmail.com, daniele.castellani@ospedaliriuniti.marche.it (D. Castellani), edoardo.agostini4@gmail.com (E. Agostini), Luciano.burattini@ospedaliriuniti.marche.it (L. Burattini), dellatti@hotmail.com (L. Dell'Atti).

<https://doi.org/10.1016/j.eucr.2021.101660>

Received 23 February 2021; Accepted 22 March 2021

Available online 25 March 2021

2214-4420/© 2021 The Authors.

Published by Elsevier Inc.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

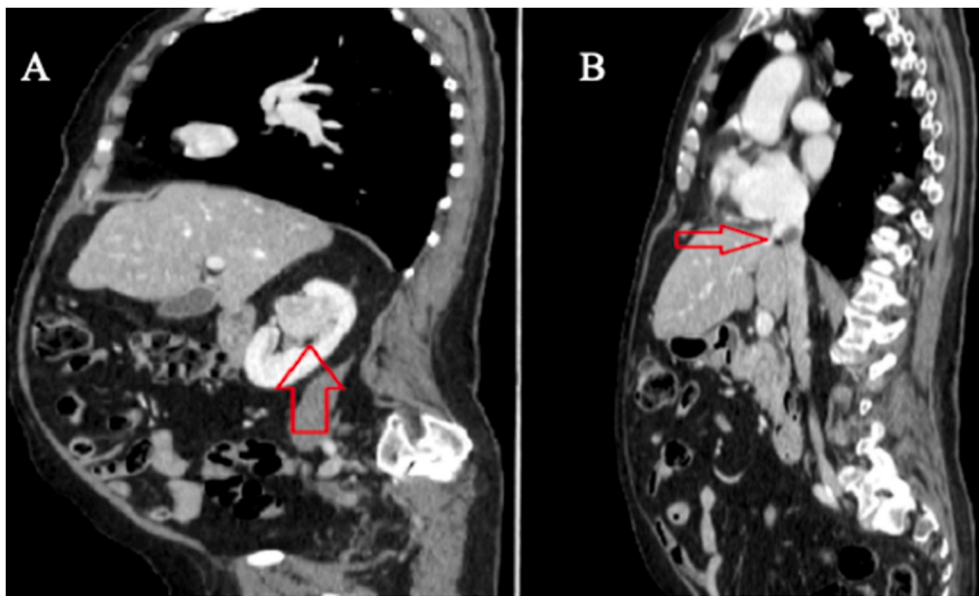


Fig. 1. Enhanced computed tomography shows A) right kidney tumor (red arrow); B) tumor thrombus extending in the right atrium (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

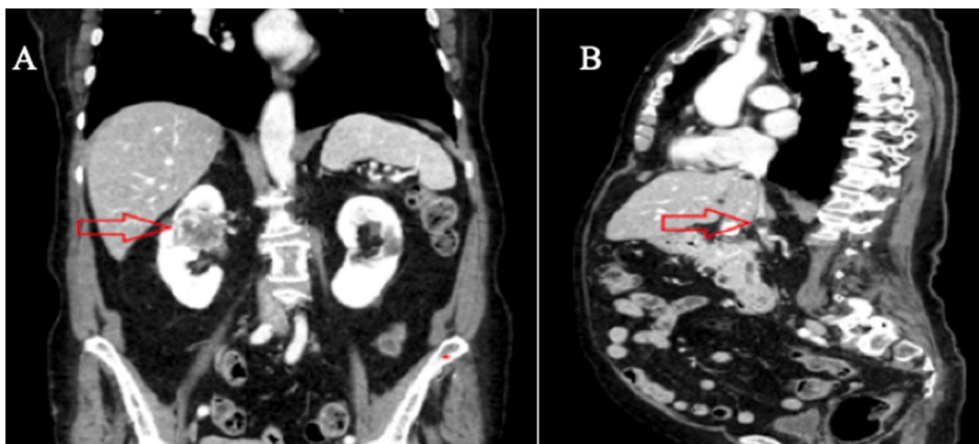


Fig. 2. Enhanced computed tomography six months after systemic therapy with pazopanib. A) minimal downsizing of the kidney tumor (red arrow); B) downstaging of the tumor thrombus located 5 cm below diaphragmatic hiatus (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

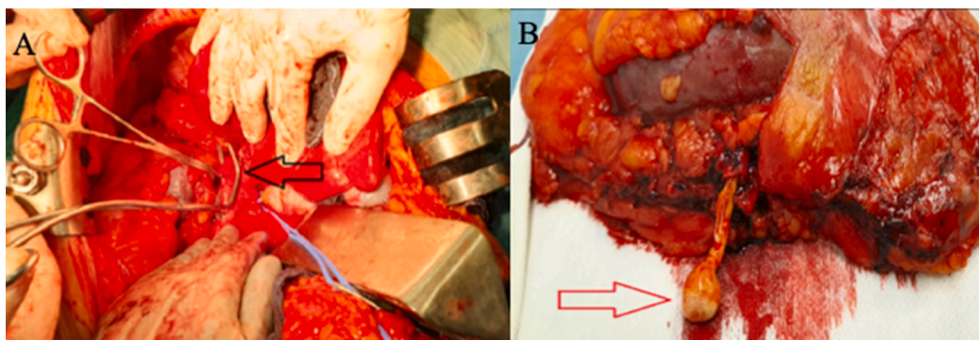


Fig. 3. A) right nephrectomy with minimal cavotomy (black arrow); B) removed thrombus (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Discussion

Aggressive surgical therapy remains the cornerstone of curative treatment of non-metastatic patients who have at presentation tumor thrombus extension above the level of the hepatic veins (level III-IV). Level IV tumor thrombus is a significant predictor of 90-day major postoperative complications that occur in up to 60% of patients.^{1,3} Nevertheless, level IV tumor thrombus is not a predictor of poor overall survival and surgical thrombus extirpation should be offered.³ Indeed, only poor performance status and metastatic disease at presentation have been shown to predict lower overall survival in such patients.³ However, there are no reliable comparative data regarding the impact of extent of thrombus removal on survival, with some studies highlighting that a complete thrombus removal did not affect prognosis.² Besides, elderly patients with comorbidity are usually unfit to undergo major cardiac surgery. Therefore, urologists deal with patients with a level IV thrombus who require aggressive surgery that cannot be safely offered because of poor performance status. In this complex scenario, neoadjuvant systemic therapy can be helpful for two reasons. First, systemic targeted therapy is the current standard treatment of metastatic clear-cell RCC and it can be useful in treating occult micro-metastasis that are present in up to 60% of RCC patients with tumor thrombus. Second, targeted therapy has a cytoreductive effect on the primary tumor and it may decrease the tumor thrombus burden, improving the feasibility of nephrectomy and thrombus resection. This was the case of our patient who was unfit for surgical resection in extracorporeal circulation and deep circulatory arrest. She was started on pazopanib and after eight months the reduction of disease burden allowed her to undergo radical nephrectomy with minimal cavotomy and thrombus resection. The relevance of our case lies in two aspects. First, half a dose of pazopanib had an efficient cytoreductive effect on thrombus size and extension. Indeed, older patients with RCC are more disposed to side effects of targeted therapy and dose modification has been demonstrated to reduce toxicity while maintaining efficacy.⁴ A lower rate of toxicity also permits patients to keep going on therapy with a better quality of life. The second important aspect of our case was the meaningful downstaging of the tumor thrombus from level IV to level II that changed the surgical approach from a sternotomy with cardio-pulmonary bypass to a marginal cavotomy with an acceptable bleeding and eventful postoperative course. Nevertheless, there is a paucity of data on tumor thrombus downstaging among patients with no metastatic disease after systemic targeted therapy. Okamura et al. showed that neoadjuvant pazopanib was effective in tumor thrombus downstaging in 7 out of 9 patients. Among these seven patients, four avoided sternotomy and the remaining three avoided hepatic mobilization and hepatic vein clamping.⁵ An accurate patient selection for neoadjuvant therapy is mandatory in this setting to offer preoperative systemic treatment to patients with a high chance of benefit and to avoid surgery delay in patients with a low probability of response. According to the currently available data, neoadjuvant targeted therapy should be offered to patients with level III-IV tumor thrombus, tumors larger than 7 cm in solitary kidney with tumor not feasible for nephron-sparing

surgery, and patients with impaired cardiac and pulmonary function.⁵ Conversely, patients with lymph node metastasis, a high neutrophil count and a not clear cell RCC have limited benefit from neoadjuvant systemic targeted therapy.⁵

Conclusions

The present case demonstrated that an course of a reduced dose of pazopanib was effective in downstaging the tumor thrombus from level IV to level II, allowing the patient to undergo a complete tumor clearance without the needing for cardiac surgery and with an eventful postoperative course.

CRedit author statement

AB Galosi, L Burattini, A Papaveri: Conceptualization; D Castellani, A Papaveri: Writing- Original draft preparation. E Agostini, L Burattini: Investigation, Acquisition of data. L Dellatti: Writing- Reviewing.

Consent

Informed consent was obtained in both written and verbal forms from the patient to publish this case report and any accompanying images.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

None.

References

- Blute ML, Leibovich BC, Lohse CM, Cheville JC, Zincke H. The Mayo-Clinic experience with surgical management complications and outcome for patients with renal cell carcinoma and venous tumour thrombus. *BJU Int.* 2004;94(1):33–41. <https://doi.org/10.1111/j.1464-410X.2004.04897.x>.
- Lardas M, Stewart F, Scrimgeour D, et al. Systematic review of surgical management of nonmetastatic renal cell carcinoma with vena caval thrombus. *Eur Urol.* 2016;70(2):265–280. <https://doi.org/10.1016/j.eururo.2015.11.034>.
- Haddad AQ, Leibovich BC, Abel EJ, et al. Preoperative multivariable prognostic models for prediction of survival and major complications following surgical resection of renal cell carcinoma with suprahepatic caval tumor thrombus. *Urol Oncol Semin Orig Investig.* 2015;33(9):388. <https://doi.org/10.1016/j.urolonc.2015.04.010.e1-388.e9>.
- Hermansen CK, Donskov F. Outcomes based on age in patients with metastatic renal cell carcinoma treated with first line targeted therapy or checkpoint immunotherapy: older patients more prone to toxicity. *J Geriatr Oncol.* 2020. <https://doi.org/10.1016/j.jgo.2020.12.008>. Published online December.
- Okamura Y, Terakawa T, Sakamoto M, et al. Presurgical pazopanib improves surgical outcomes for renal cell carcinoma with high-level IVC tumor thrombosis. *In Vivo.* 2019;33(6):2013–2019. <https://doi.org/10.21873/invivo.11698>.