

# Intravenous caval leiomyomatosis in the setting of renal cell carcinoma – A case report

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## ARTICLE INFO

### Keywords:

Intravascular leiomyomatosis  
Renal cell carcinoma  
Translocation  
Thrombectomy  
Nephrectomy  
Pulmonary embolectomy

## ABSTRACT

Uterine leiomyomas are common, benign neoplasms of the uterine smooth muscle. Leiomyomatosis is uncommon and causes development of multiple leiomyomas that can manifest as intravascular leiomyomatosis (IVL). We present the case of a 46-year-old female with IVL extending from the right gonadal vein to the right atrium and pulmonary arteries with an independent renal cell carcinoma of the right kidney. She underwent successful open right radical nephrectomy, inferior vena caval tumor thrombectomy and pulmonary embolectomy. While there was initial concern for hereditary renal cell carcinoma, final histologic testing did not support the diagnosis.

## 1. Introduction

While leiomyomas of the uterus are common, intravascular leiomyomatosis is a rare manifestation in which inferior vena cava (IVC) with intracardiac extension has been described in less than 100 cases.<sup>1</sup> These tumors are typically slow growing, arise from the gonadal vessels and can result in lower extremity swelling, pulmonary emboli, cardiac failure, and sudden death in some cases. Patients may not have symptoms until the mass becomes intracardiac. Similarly, renal cell carcinoma (RCC) can invade the renal vein and IVC, but the incidence of vascular invasion is much more common and reported in 10% of cases.<sup>2</sup>

Hereditary leiomyomatosis renal cell carcinoma (HLRCC) is a rare genetic autosomal dominant germline mutation resulting in loss of fumarate hydratase (FH) expression and overexpression of modified cysteine-S-(2-succino)-cysteine (2SC). Patients develop multiple uterine and subcutaneous leiomyomas and prognosis is often poor.<sup>3</sup> Intravascular leiomyomatosis and the presence of a renal tumor in our young patient raised concerns for HLRCC; however, we report a unique case of translocation-associated RCC and concomitant IVL with right atrial and pulmonary artery extension.

## 2. Case report

A 46-year-old African American female was diagnosed with a large right pulmonary artery (PA) embolism believed to be related to an uncomplicated admission for COVID. Despite anticoagulation, normal right heart and PA pressures, repeat imaging demonstrated a persistent pulmonary thrombus with calcifications. She later presented with abdominal pain, constipation, and dyspnea. Abdominal imaging demonstrated a 25 cm retroperitoneal mass extending from the right gonadal vein to the retrohepatic IVC with 5 cm of intracardiac right atrial (RA) extension. Additionally, a 3.7 cm, heterogenous, enhancing, central right renal mass in discontinuity with the IVC mass was noted (Fig. 1a); the right renal vein was tumor free. She had a history of abdominal hysterectomy for multi-focal leiomyoma 4-years prior. These two factors raised suspicion for intravascular leiomyoma as opposed to RCC.

After normal left heart catheterization, the patient was taken to surgery with urologic oncology and cardiothoracic services. A midline laparotomy extending to sternotomy was performed simultaneously. The entire right colon, duodenum, right kidney, liver, IVC and right gonadal vein were mobilized (Fig. 1b). Intraoperative ultrasound demonstrated that the tumor appeared mobile and non-adherent. The right renal hilum was taken with a vascular staple load and the kidney

**Abbreviations:** IVL, Intravascular leiomyomatosis; IVC, Inferior vena cava; RCC, Renal cell carcinoma; HLRCC, Hereditary leiomyomatosis renal cell carcinoma; FH, Fumarate hydratase; 2SC, cysteine-S-(2-succino)-cysteine; PA, Pulmonary artery; RA, Right atrial; MTF, Microphthalmia transcription factor.

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<https://doi.org/10.1016/j.eucr.2022.102175>

Received 17 June 2022; Accepted 23 July 2022

Available online 31 July 2022

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was removed.

The patient's aorta, SVC and infra-renal IVC below the right gonadal vein were cannulated for cardiopulmonary bypass. Vascular clamps were placed on the infrarenal IVC, left renal vein and hepatic triad (Pringle maneuver). After initiating bypass, a cavotomy was made encircling the os of the right gonadal vein and extending cranially to the retrohepatic cava. The intravascular mass was soft, non-adherent and easily removed by pushing the right atrial component downwards and pulling from below. The cavotomy was closed and clamps removed. Next, after arrest and cardioplegia, the right PA was opened, and the tumor was removed entirely. The PA was repaired. Ultrasound confirmed removal of all intravascular tumors. After restoration of spontaneous circulation, the patient was closed, had an uneventful recovery and discharged on post-operative day eight. She was last seen 11 months postoperatively and was doing well without evidence of recurrence on imaging.

The IVC tumor measured 17 cm with additional tumor in the RA and PA (Fig. 1c). Microscopically, the tumor was composed of elongated spindle cells with eosinophilic cytoplasm. No cytologic atypia or necrosis were noted; mitotic figures were low. Immunohistochemical stains for SMA, caldesmon and desmin were positive, supporting the smooth muscle origin (Fig. 2).

The kidney tumor measured 3.5 cm and margins were negative. Microscopically, the tumor showed compact architectural growth patterns and rare papillary formation. Tumor cells were large with clear to eosinophilic cytoplasm. Tumor cells showed retained FH and SHDB expression and were negative for 2SC. Cathepsin K was positive (Fig. 3). Renal Cell Carcinoma Fusion Gene Analysis by Archer FisionPlex demonstrated a *MALAT1-TFEB* rearrangement.<sup>4</sup> In view of the morphological, immunohistochemical and molecular profile, a diagnosis of microphthalmia transcription factor (MITF) family translocation-associated RCC was concluded.

### 3. Discussion

Herein we report the first reported case of IVL with intracardiac extension and pulmonary arterial embolization with concomitant localized RCC. While her disease was extensive, the tumor thrombus and pulmonary emboli were successfully removed in a single stage procedure by urology and cardiothoracic surgery. Interestingly, while HLRCC is characterized by cutaneous and uterine leiomyomas as well as increased risk of RCC with papillary features, our patient was not diagnosed with

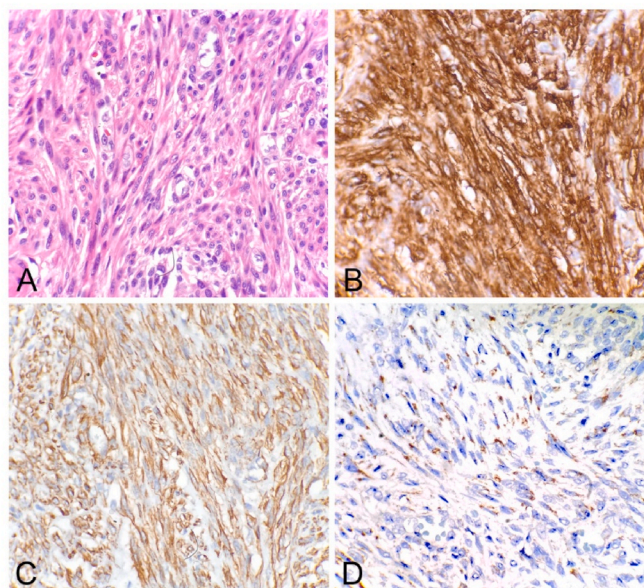


Fig. 2. Intravenous tumor composed of bland spindle cells (A) positive for SMA (B) and caldesmon (C), supporting the smooth muscle nature. FH expression was retained (D).

HLRCC or have a family history suspicious for HLRCC.

The kidney tumor in our patient showed focal papillary architecture in addition to cells with clear and eosinophilic cytoplasm, raising an initial differential of clear cell RCC, papillary RCC, and chromophobe RCC. However, positivity for cathepsin K argued against these diagnoses. The combination of the morphologic characteristics and positivity for cathepsin K steered us towards an MITF family translocation-associated RCC. Further molecular analysis showed *MALAT1-TFEB* rearrangement, supporting the diagnosis of MITF family translocation-associated RCC, associated with a 10% mortality rate.<sup>5</sup>

### 4. Conclusion

Intravascular leiomyomatosis with intracardiac extension, although rare, is associated with a significant mortality if not addressed promptly. In the context of leiomyomatosis, the presence of a renal tumor in a

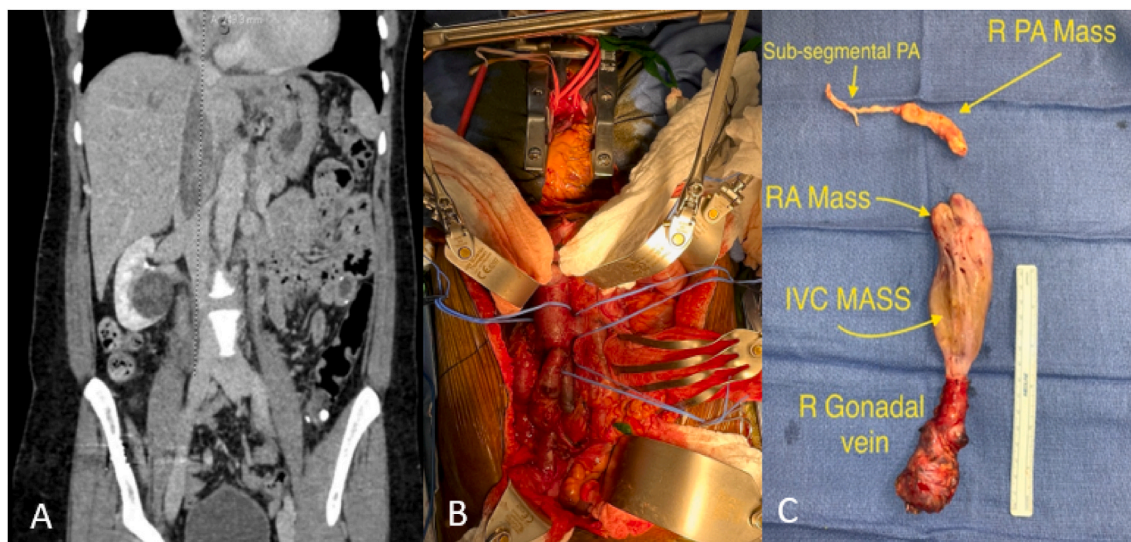
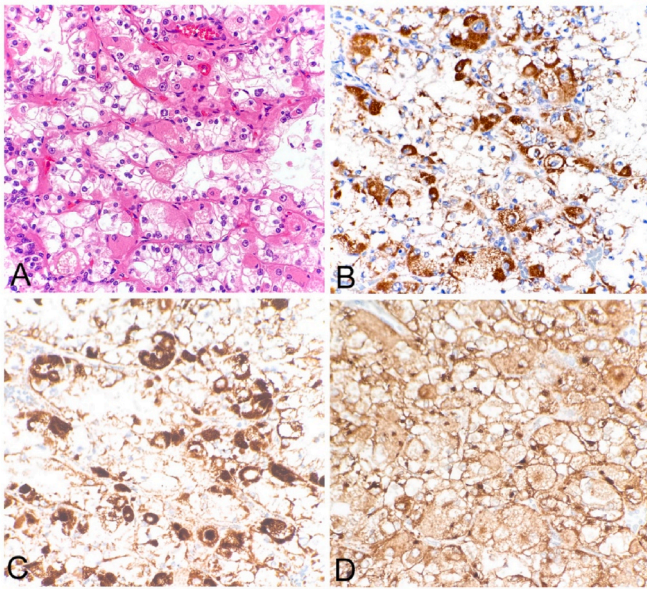


Fig. 1. Computed tomography with intravascular contrast (1A) and intraoperative demonstration (1B) of the extent of tumor thrombus. (1C) Resected IVC and right atrial tumor thrombus as well as a separate right pulmonary arterial and subsegmental thrombus.



**Fig. 3.** Kidney tumor composed of cells with clear and eosinophilic cytoplasm, round to oval nuclei with prominent nucleoli (A). FH (B) and SDHB (succinate dehydrogenase B) (C) expression are retained. Cathepsin k is positive (D).

young patient should raise concern for FH-deficient RCC, an often-

aggressive tumor. We are instead reporting an unusual case of TFEB-rearranged RCC which shows a more indolent behavior. While outcomes of TFEB-rearranged RCC have generally been favorable, aggressive subsets have been known to occur. Lastly, this case serves as a model of complex, multidisciplinary surgical coordination, utilizing the expertise of urologic oncology and cardiothoracic surgery.

#### 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

There are no competing interests to disclose.

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