

Radical Nephrectomy and Pulmonary Lobectomy for Renal Cell Carcinoma With Tumor Thrombus Extension into the Inferior Vena Cava and Pulmonary Arteries

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Abstract. *Background/Aim:* Renal cell carcinoma (RCC) is one of the most common malignancies of the urinary tract. Venous migration, tumor thrombus and metastases are often seen in patients with RCC and are adverse prognostic factors. Intravascular tumor growth along the renal vein into the inferior vena cava occurs in up to 10% of all patients with RCC. Furthermore, extension of the tumor reaching the right atrium is detected in approximately 1% of all patients. Synchronous involvement of pulmonary arteries with tumor emboli is very rare and challenging. Management of metastatic RCC includes surgical resection of renal and metastatic lesions. We present 3 cases of patients with RCC tumor thrombus extending into the inferior vena cava (IVC) and with pulmonary emboli of the tumor thrombus into one of the branches of the main pulmonary artery. All the cases had simultaneous resection of the kidney tumor with the tumor thrombus and pulmonary lobectomy that included the tumor emboli with satisfactory outcome. *Case Report:* We present a series of cases of RCC with tumor extension into the inferior vena cava (IVC) and with tumor emboli to the pulmonary arteries. Surgical procedure in all cases consisted of radical nephrectomy with IVC tumor thrombus resection, along with a thoracotomy with lung resection including the tumor emboli to one of the branches of the main pulmonary artery. Synchronous metastatic lesions were found on the liver in one case and contiguous extension of renal tumor to

the pancreas in another. *Conclusion:* In patients with IVC thrombus with synchronous pulmonary artery tumor embolus, such as the cases presented in this series, a careful multidisciplinary management approach is preferable. Transplant technique used in our open approach minimizes complications, blood loss, and provides excellent visualization for abdominal vascular manipulation of IVC. This provides a potentially curable treatment option with acceptable survival rates.

Renal cell carcinoma (RCC) is one of the most common malignancies of the urinary tract. RCC accounts for 3% of all adult cancers and it is the twelfth most common cancer in the world (1). RCC is more prevalent in men and risk factors for RCC include smoking, obesity and hypertension (2). Venous migration, tumor thrombus and metastases is often seen in patients with RCC and are adverse prognostic factors (3). Intravascular tumor growth along the renal vein into the inferior vena cava occurs in up to 10% of all patients with RCC (4). Furthermore, extension of the tumor reaching the right atrium is detected in approximately 1% of all patients (5). Synchronous metastatic disease is presented in about one third of newly diagnosed cases (6). Management of metastatic RCC includes surgical resection of renal and metastatic lesions. We present 3 cases of patients with RCC tumor thrombus extending into the inferior vena cava (IVC) and with pulmonary emboli of the tumor thrombus into one of the branches of the main pulmonary artery. All the cases had simultaneous resection of the kidney tumor with the tumor thrombus and pulmonary lobectomy that included the tumor emboli.

Case Report

Ethics approval and consent to participate. Ethics committee approval was obtained from Institutional Review Board (IRB) at University of Miami.

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Key Words: Renal cell carcinoma, inferior vena cava, thrombus, pulmonary embolism, radical nephrectomy, lung metastasis.



Figure 1. Contrast enhanced abdominal computed tomography (CT) with a heterogeneous mass in the left kidney (arrow) with a filling defect in the renal vein suggesting tumoral invasion (arrowhead).

Case 1. A 33-year-old female patient without significant medical history presented to the Emergency Department with left flank pain and visible hematuria. Imaging studies with computerized tomography (CT) and magnetic resonance imaging (MRI) reported a large left renal tumor with tumor thrombus extending to renal vein (Figure 1). Due to the clinical suspicion of pneumonia, a contrast-enhanced chest CT was performed which showed mild right pleural effusion and a pulmonary embolism (PE) in the right pulmonary artery, likely from the tumor (Figure 2). There was no evidence of additional lesions in the abdomen or thorax. A left subcostal incision with some extension to the right side was made and medial mobilization of colon, pancreas, and left kidney was performed in order to ligate left renal artery (7). We continued the dissection of the renal vein and vena cava with partial clamping of the IVC. The IVC was opened to remove the tumor thrombus with subsequent vascular repair with 4-0 Prolene and *en bloc* removal of the surgical specimen (Figure 3). Inspection of the liver showed a small 1 cm nodule which was resected. During the abdominal wall closure, a transesophageal echocardiogram (TEE) was performed without evidence of tumor thrombus in the right atrium and the main pulmonary arteries. The thoracic team proceeded with right thoracotomy. The location of the PE was distal in the branches of the right lower lobe pulmonary artery (PA). After right posterolateral incision, the right lower lobe was exposed as well as the area of infarction. A longitudinal arteriotomy was made on the PA through which some of the embolized tumor was extracted. However, the majority of the distal tumor was firmly attached to the vessel wall and it was impossible to excise them without significant damage of the pulmonary artery branches. It was decided to proceed with right lower lobectomy with complete tumor removal (Figure 4). Pathological analysis of

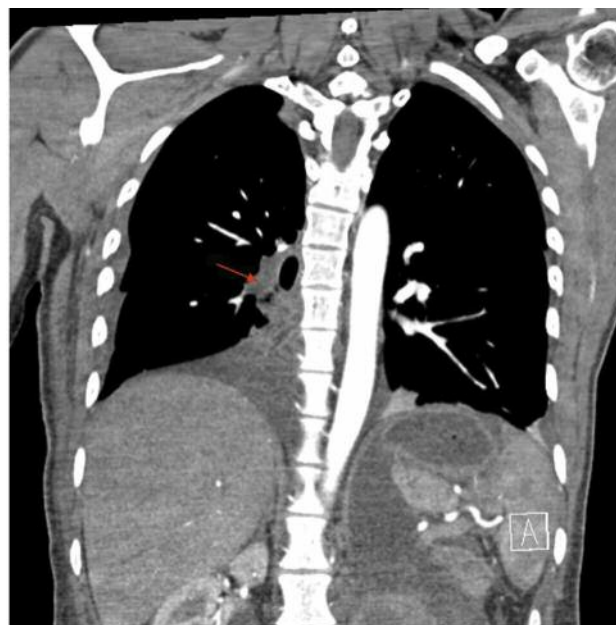


Figure 2. Contrast enhanced chest computed tomography (CT) with defect in contrast filling in the right pulmonary artery (red arrow) compatible with pulmonary embolism.

the kidney and lung indicated metastatic RCC and is shown in Table I. The procedure was completed without further complications and did not require blood transfusion. The patient recovered uneventfully and was discharged on the 8th post-operative day.

Case 2. A 70-year-old woman with history of high blood pressure and coronary vascular disease, presented to the Emergency Department with shortness of breath and cough. Imaging studies of the chest, a left lower pulmonary embolus was detected. Further workup revealed large right renal mass with level IIIb IVC thrombus with hepatic vein tumor involvement (8). We proceeded with right subcostal incision and medial mobilization of the right kidney to ligate the right renal artery (7). A transplant-based technique was employed to mobilize the liver off the IVC in a piggyback fashion (9). A plane of dissection between the IVC and posterior abdominal wall was developed with ligation of any venous collaterals. Complete circumferential control of the IVC was achieved. The infra renal IVC and contralateral renal vein were clamped, the tumor thrombus was milked below the major hepatic vein and vascular clamp was applied. A cavotomy was performed with *en bloc* removal of the tumor thrombus with the right kidney. TEE was performed to assure no pulmonary emboli occurred during the kidney tumor resection.

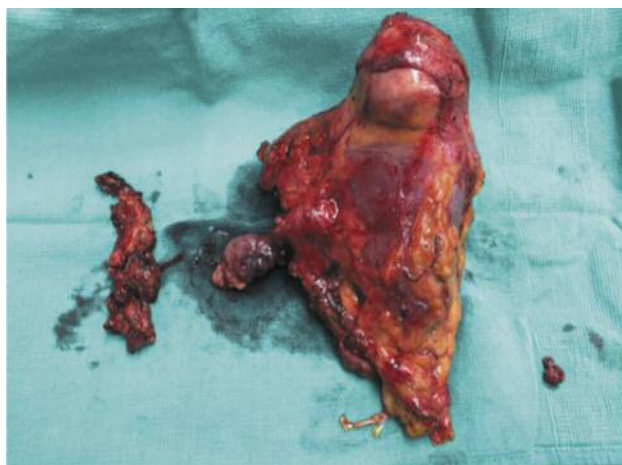


Figure 3. Left kidney specimen with renal tumor in the upper pole. Tumor thrombus invading corresponding space for renal vein and inferior vena cava.



Figure 4. Specimen of right lower pulmonary lobe with vascular ligation for tumoral pulmonary embolism.

Table I. Characteristics of cases with renal cell carcinoma with inferior vena cava invasion and distal pulmonary embolism.

Cases	Age	Gender	Pathology	Level of extension of TT	Tumor size	Fuhrman nuclear grade	Extrarenal invasion	AJCC staging	Surgical management	Post-operative follow-up
1	33	F	Clear RCC	IIIa	8 cm	III	Metastasis to the lung and liver	pT3, N0, M1	Left radical nephrectomy + right lower lobe lobectomy	Died after 48 months
2	70	F	Clear RCC	IIIa	7.8 cm	IV	Metastasis to the lung	pT3b pN0, M1	Right radical nephrectomy + left lower lobe lobectomy	Alive and disease free at 60 months
3	56	F	Clear RCC	II	10.5 cm	II	Metastasis to the lung, local spread to pancreas	pT4, pNx, pM1	Left radical nephrectomy + Resection <i>en bloc</i> of spleen and distal pancreas + left upper lung sleeve lobectomy	Lost for follow-up after 36 months

RCC: Renal cell carcinoma, PE: pulmonary embolism, TT: tumor thrombus, AJCC: American Joint Committee on Cancer.

After abdominal closure, the thoracic team performed a left thoracotomy and proceeded with main pulmonary artery dissection with arteriotomy; samples for pathology were obtained which confirmed metastatic necrotic RCC inside the arterial lumen. Following this, left lower lobectomy was performed. Post-operative course was uneventful. Patient was discharged on day 10 without complications.

Case 3. A 54-year-old female patient was transferred to our Institution with atelectasis of the left lung (Figure 5). CT scan and MRI showed a large left renal mass with level IIIa retro hepatic IVC tumor thrombus (Figure 6) (8). Bronchoscopy revealed an occluding left bronchus endoluminal tumor at 5 cm from the carina. Biopsy was

consistent with metastatic RCC. The patient was scheduled for a left upper lobe sleeve lobectomy with mediastinal lymph node dissection. The procedure was performed by the thoracic team without complications. After the thoracotomy, radical nephrectomy with tumor thrombus resection was performed. Before incision, a TEE was performed to verify that the right atrium and pulmonary arteries were clear of the tumor. We proceeded with bilateral subcostal incision, and started with mobilization *en bloc* of left kidney, pancreas and spleen with posterior ligation of renal artery for vascular control of the tumor (7). The renal tumor extended to the pancreas tissue without a surgical plane, therefore, distal pancreatectomy and splenectomy was performed (Figure 7). The IVC was dissected in a similar fashion as described in

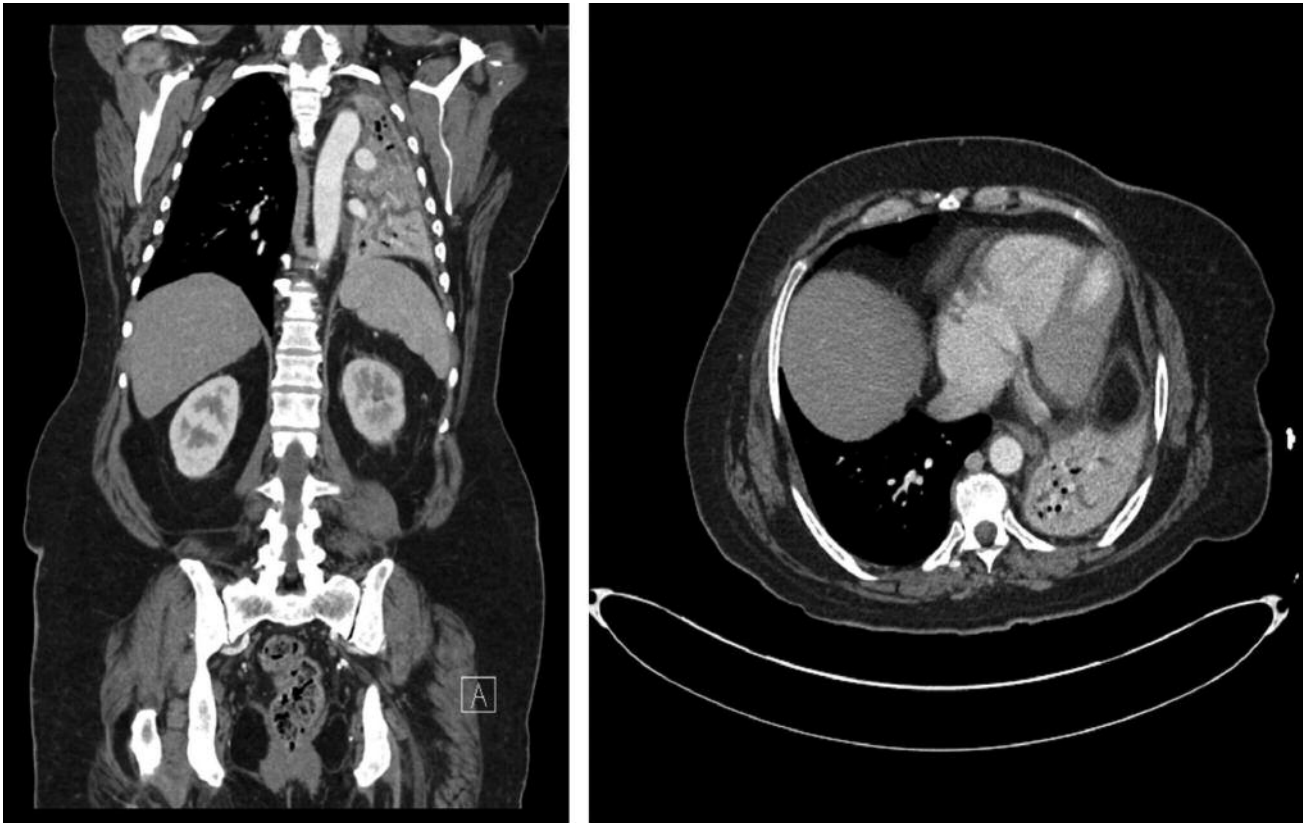


Figure 5. Chest CT scan with complete collapse of the left lung with heterogeneous enhancement of the left lung parenchyma and several foci of entrapped air within dilated peripheral bronchi.

case 2. The right renal vein, right adrenal vein and IVC was secured and clamped. Then, we proceeded to do a TEE to delineate the thrombus. A cavotomy and thrombus removal was performed *en bloc* with removal of left kidney. The procedure was completed without complications. Patient was discharged on the 7th post operative day. Patient follow-up is presented in Table I.

Discussion

RCC is one of the most common urological malignancies with approximately 74,000 new cases diagnosed every year in the United States while around 15,000 patients die from disease annually (10). The incidence of RCC has been increasing in the US and worldwide, partly because of the increased use of diagnostic image testing for unrelated conditions. Surgical removal remains the backbone strategy for treatment of RCC. Approximately 25% of RCC patients present with advanced disease at the time of diagnosis (11). A unique feature of RCC is the tropism for blood vessel extension, involving renal vein and IVC in 10% of cases and extension in to the right atrium in 1% of cases (12). Distant

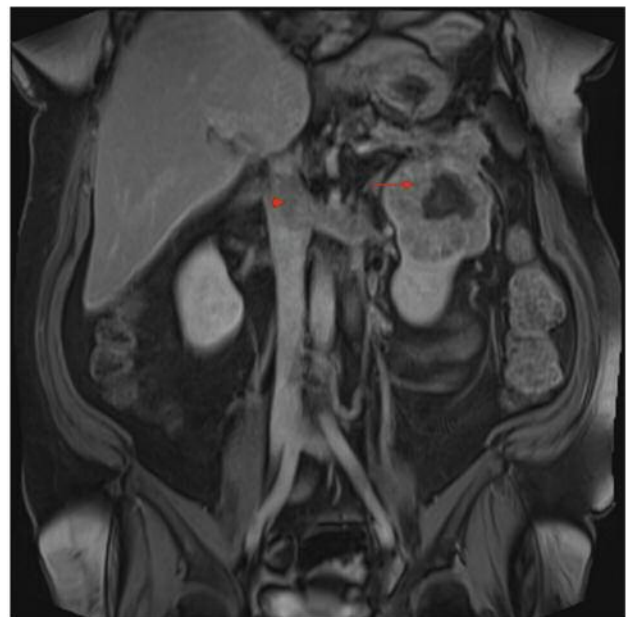


Figure 6. Abdominal MRI with left tumoral mass in upper pole (arrow) with renal vein and IVC tumoral thrombus (arrowhead).

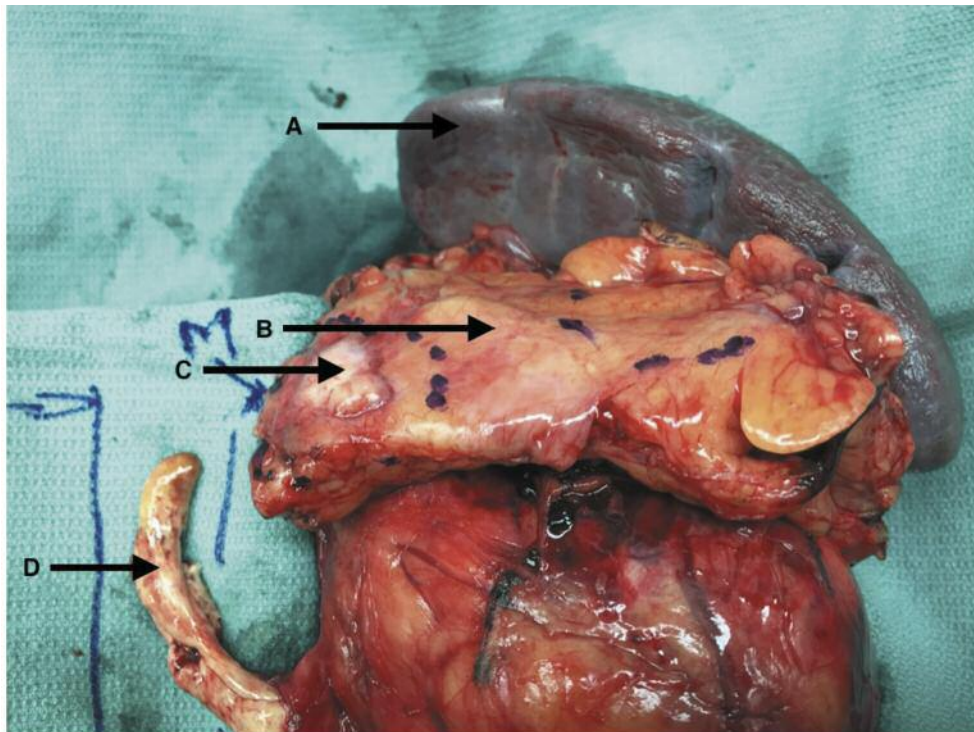


Figure 7. Specimen of kidney with renal mass with en bloc resection of spleen (Arrow A), distal pancreas (Arrow B), pancreatic mass (Arrow C) and tumor thrombus in IVC (Arrow D).

metastasis to the lung or liver can be present in 29-55% of patients with vascular involvement (13, 14). Among the organs where metastasis occurs, lung is the most common site with 30% of patients eventually developing extra tumoral disease (15). According to studies on RCC metastasis, outcomes after lung metastasis show a median survival of 43.3 months with estimated 5-year survival of 51.4% after lung metastasis resection (16).

Complete staging of RCC with imaging studies is required as in most cases metastatic deposits do not cause clinical symptoms. The complete clinical staging and assessment is of utmost importance to determine the stage and extension of the tumor to choose appropriate therapy. The treatment options consist broadly from partial nephron sparing nephrectomy, to total radical nephrectomy with tumor thrombectomy and metastasectomy and in some cases systemic therapy. In cases of tumor extension through the vasculature, prompt intervention and planning must be done with interdisciplinary approach. There are four levels of extension of RCC tumor thrombus according to the classification of IVC tumor thrombus levels according to the Mayo (Novick) staging system (17). In this classification; level I TT has renal vein extension to 2 cm proximal of IVC, level II IVC involvement below hepatic veins, level III has

TT from the kidney to the IVC below the diaphragm and lastly level IV has TT extending to right cardiac chambers. In the Miami Classification system, special interest is placed in the exact location of the tumor behind the liver and in anatomic reference to the hepatic veins. In this system, for RCC in conjunction with IVC tumor thrombus, level IIIa tumors are defined as those with thrombus extending into the retrohepatic IVC but ending below the origins of the major hepatic veins, level IIb as extending to the ostia of the major hepatic veins, level IIIc as extending above the major hepatic veins but below the diaphragm, and level IIId as extending above the diaphragm but not into the right heart (8). The goal should remain to remove the tumor with radical nephrectomy (RN) and complete tumor thrombectomy (TT) (18). RN with TT is an extensive surgery with an estimate 10% mortality rate and multiple complications (19). Over the last decades the morbidity and mortality of this operation has decreased making it acceptable as the mainstay treatment. Under the current surgical approach there is a 5-year survival rate of 69% in patients without metastasis (20, 21).

The use of extracorporeal circulation, use of transplant techniques for liver mobilization, and combined abdominal and thoracic approaches have decreased the mortality of the RN with TT (22). The use of extra corporeal circulation helps in

the manipulation of vascular structures to release tumoral burden, nevertheless is accompanied by systemic inflammatory response and may contribute to morbidity of the procedure. Another technique described by our group consist of the use of transplant techniques for mobilization of the liver from the vena cava using the piggyback technique in order to preserve normal blood flow and obtain complete visualization of vena cava. In 1994, the experience gained with liver transplant and abdominal organ procurement permitted Marsh et al. from the University of Washington to introduce the concept of applying the transplant- based approach to complex cases in urologic oncology (23, 24). The main objective of our group in utilizing transplant techniques was to decrease blood loss and transfusion rates associated with commonly uncontrollable bleeding from different venous collaterals generated in response to IVC occlusion (caused by tumor thrombus), despite the fact that, at this moment, much had already been advanced in this aspect by the use of “piggy-back” liver mobilization. By reinforcing the basic principles of visceral rotation taken from Cattell et al., a posterior approach to the main renal artery was described in order to delay the dissection of the engorged collaterals until the primary tumor was deprived of blood flow, thus, causing collateral decompression, facilitating its handling, and decreasing the chance for bleeding (23, 25). Moreover, Ciancio et al. refined the technical aspects of IVC handling, interruption, resection, and reconstruction to further decrease the risk of blood loss and to solve the remaining problems regarding perioperative embolization and venous drainage after the procedure (9, 14).

Usually, when TT is extensive, the venous flow is preserved through alternate venous drainage to the right atrium. This contributes to hemodynamic stability when the vena cava is clamped in transplant technique (9, 26). Special attention needs to be placed in this technique when liberating the vena cava ligament to prevent PE on its release (27). Use of intra operative trans esophageal echocardiogram is of utmost importance for monitoring TT residual mass in major vessels as well as to visualize cardiac chambers for the presence of tumor emboli. The surgical approach must be based on expertise of the team and intent to remove the tumor completely. In all our cases, a transplant technique was employed which allowed for vascular control, ample visualization of lesions such as liver metastasis resection in case 1, lymph node dissection, and complete tumor thrombus extraction from IVC.

During the radical nephrectomy procedure, manipulation of the renal mass can be considerable. This along with vascular clamping and arterial flow deprivation after ligature can cause dislodgement of tumoral mass from main tumor and cause PE of various degrees of severity. PE in this setting is a dreaded complication that can be present in 3% of the cases with a mortality rate that can reach 75% (28). In the setting of tumoral PE, the embolectomy is performed since the embolus is the tumor itself composed of neoplastic

cells. In our patient, synchronous lesions in other organs were resected in liver, pancreas, and lung in the same procedure. Most common organs for RCC metastases are the lungs (60-75%), lymph nodes (60-65%), liver (19-40%), bone (39-40%), and brain (5-7%) (29). There exists data where 20-40% of patients with localized disease at diagnosis eventually develop metastasis, with an estimated overall survival rate of 35 to 50% after resection of lesions (30).

The development of robotic surgery in urology has pushed for the use of these minimal invasive techniques for management of RCC with TT. In some series, the use of robotic surgery for level II IVC thrombectomy demonstrated decreased hospital stay and similar 30-day mortality compared to open approach (31). Reports for more advanced level of TT IVC involvement may be anecdotal but in experienced hands and selected cases, robotic approach offers a reasonable alternative to open surgery (32).

Conclusion

RCC has a spectrum of clinical presentations ranging from local to systemic disease with vascular infiltration and synchronous distant metastasis. Surgery represents the first line of treatment and every attempt should be made to remove the entire tumor burden. In patients with extensive disease such as the cases presented in this series, a careful diagnostic approach and multidisciplinary management with urologists, thoracic surgeons, radiologists and pathologists is preferable. Transplant technique used in our open approach minimizes complications, blood loss, and provides excellent visualization for abdominal vascular manipulation of IVC. Extensive disease can be treated with metastasectomy as needed with lung lobe resection and liver metastasectomy. This provides a potentially curable treatment option with acceptable survival rates.

Conflicts of Interest

The Authors declare no conflicts of interest.

Authors' Contributions

AM participated in manuscript preparation and analyzing the data. AL participated in manuscript preparation and analysis of the surgical procedure. GC was responsible for overall manuscript, data maintenance and surgical management. All Authors read and approved the final manuscript.

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