Surgical excision of renal cell carcinoma with caval and intra-atrial tumour thrombus extension using deep hypothermic circulatory arrest

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Abstract
Surgery for tumour thrombus extension in Renal Cell Carcinoma may be associated with a good prognosis if no distant metastases are identified and if the thrombus can be completely excised. The surgical approach chosen will depend on the level of tumour thrombus extension. We present a case of Renal Cell Carcinoma in the right kidney with tumour thrombus extension into the right atrium. This was successfully removed by right radical nephrectomy and excision of the atrial thrombus using cardio-pulmonary bypass and deep hypothermic circulatory arrest. This is the first procedure of its kind to be undertaken in Malta.

Keywords
Renal cell carcinoma, Atrial tumour thrombus, Surgery, Cardio-pulmonary bypass, Deep hypothermic circulatory arrest

Introduction
Some cases of renal cell carcinoma (RCC) may be very aggressive. One of the features underlying this is their propensity for vascular invasion. Renal Vein (RV) or Inferior Vena Cava (IVC) extension occurs in 4 to 10% of cases. Very rarely tumour thrombus may extend all the way above the diaphragm and into the right atrium. In 1972, Skinner et al. first reported that caval tumour thrombus extension in renal cell carcinoma is potentially curable if complete excision can be achieved. The surgical approach chosen will depend on the level of tumour thrombus extension. The higher the level, the more complex the surgical technique becomes, often requiring a multidisciplinary approach. Careful pre-operative staging and planning of surgery is paramount to a successful outcome.

We present a case of right kidney RCC with intra-atrial tumour thrombus extension successfully treated by radical nephrectomy and excision of the thrombus from the right atrium using cardio-pulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA). This is the first procedure of its kind to be undertaken in Malta.

Case Presentation
A 59-year-old otherwise healthy male presented to the Urology Unit at Mater Dei Hospital with acute onset of right loin pain and gross haematuria. An ultrasound scan revealed a solid lesion in the lower pole of the right kidney. Further evaluation by CT Scan confirmed the presence of a large renal tumour with extension of tumour thrombus into the renal vein and intrahepatic segment of the IVC. (Figure 1a,b).
Doppler Ultrasound revealed supra-diaphragmatic extension of tumour thrombus into the right atrium. There was no evidence of any other extrarenal spread or distant metastases. Following accurate tumour staging, the surgical approach was planned in conjunction with the cardiothoracic surgical team. Tumour nephrectomy was performed via a midline laparatomy incision, giving excellent exposure of the right kidney and the IVC that was dissected up to the inferior border of the liver. The duodenum and small bowel were reflected medially off its anterior surface. The right kidney was completely mobilised on its vascular pedicle in a plane outside Gerota’s fascia. A sling was placed around the renal vein while the renal artery was divided between ligatures. At this stage the cardiothoracic team performed a median sternotomy to expose the pericardium. The ascending aorta was cannulated using a reinforced straight tipped aortic cannula and the right atrium was cannulated with a Ross atrial basket. CPB was established after full heparinisation. The patient was cooled down slowly using the CPB heat exchanger and the head was wrapped in ice slush to further protect cerebral structures. When a core temperature of 16°C was reached, blood was drained out of the patient and circulatory arrest instituted. The IVC was opened at the level of the renal vein and the cavotomy extended cephalad. The bloodless field provided excellent exposure of the thrombus which was adherent to the wall of the IVC just above the renal vein but not infiltrating it. It was dissected off bluntly at this level. The right atrium was explored by removing the atrial basket and the thrombus was released by blunt dissection through the atriotomy. The thrombus was gently delivered whole through the cavotomy in the abdomen. The thrombus measured approximately 20cm long (Figure 2).

The cavotomy was then closed using a non-absorbable vascular suture (Prolene 4/0). A schematic representation of the tumour thrombus extension, cavotomy and cannulation of the right atrium and ascending aorta for CPB is shown in Figure 3.

Total circulatory arrest lasted 23 minutes, the circulation was restored and the patient slowly rewarmed. Cardiopulmonary bypass time was 157 minutes long. When the patient was fully rewarmed, CPB was terminated and protamine sulphate was given to reverse heparinisation. Post-operative bleeding from the adrenal bed complicated the surgery. This required re-laparatomy and packing of the area. The pack was removed two days later followed by uncomplicated recovery. Histology confirmed a Fuhrman nuclear grade IV clear cell carcinoma. Sections from the thrombus showed that it also consisted of tumour cells. The patient remained disease-free for 15 months following surgery. He was then found to have local disease recurrence, though remaining asymptomatic.

Figure 1: CT showing (a) thrombus involving right renal vein (white arrowhead) and inferior vena cava (black arrowhead); (b) tumour thrombus in intrahepatic IVC (white arrowhead)

Figure 2: Tumour thrombus retrieved from the inferior vena cava and right atrium
**Figure 3**: Diagram showing tumour thrombus extension, cavotomy and cannulation of the ascending aorta and right atrial appendage for cardio-pulmonary bypass

**Discussion**

Venous extension of tumour thrombus is asymptomatic in 50 to 75% of cases because IVC obstruction is either incomplete or has occurred gradually, allowing collaterals to develop. When signs and symptoms are present they usually include lower limb oedema, distended superficial veins and a right-sided varicocele. Intra-atrial thrombus extension, as witnessed in this case, is also often asymptomatic.

Tumour thrombus usually consists of viable tumour cells extending out of the main renal tumour into the RV and IVC, though may sometimes be mixed with benign vascular thrombus. In the majority of cases this is adherent to the vascular endothelium or free-floating in the vein, and only rarely actually invades the endothelium.

Diagnosis is mainly radiological, with Ultrasound, CT, MRI and trans-oesophageal echocardiography (TOE) replacing venacavography. CT and MRI can both accurately define the upper extent of caval tumour while TOE is particularly useful when performed intraoperatively to monitor atrial thrombus and confirm its complete excision. All these modalities have their limitations particularly in diagnosing IVC wall invasion by tumour.

Accurate pre-operative staging is of paramount importance when planning surgery since the surgical approach will be determined by the cephalad extent of the tumour thrombus. Extension into the renal vein or proximal IVC can be safely managed by simple control of the IVC proximal and distal to the thrombus. Involvement of the intrahepatic portion of the IVC often requires more complex manoeuvres such as mobilisation of the right lobe of the liver to expose the retrohepatic and suprahepatic IVC. Pringle’s manoeuvre to control hepatic inflow, ligation of the lumbar veins and control of the contralateral renal vein to prevent venous back bleeding may also be required.

Excision of intra-atrial thrombus introduces greater technical difficulties. Simply cross clamping the IVC may compromise venous return with subsequent reduction in cardiac output, catastrophic hypotension and hypoperfusion of vital organs. It may also be associated with extensive haemorrhage from venous collaterals and hepatic venous congestion. These problems are overcome by performing the procedure under full cardio-pulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA) allowing more control. CPB was employed with DHCA at 16°C. Hypothermia protects vital organs during circulatory arrest. Previous data have indicated that core body temperatures of 16 °C to 18 °C are safe for periods as long as 45 to 60 minutes, yet there is no satisfactory means to accurately monitor cerebral function during surgery. Stopping the circulation provides a bloodless operating field in which to open up the IVC, and right atrium if necessary, and remove the tumour thrombus completely under direct vision. Reported disadvantages of DHCA are a prolonged time on bypass since it takes around an hour each to cool the patient to 16°C and to rewarm. There is also an increased risk of post-operative bleeding, as witnessed by this case, due to full heparinisation while on CPB, despite administration of reversing agents. There is always the risk of hypoxic organ injury, especially cerebral.

This gentleman was disease-free 15 months after surgery but then developed local recurrence. In retrospect one might argue whether such major surgery should have been undertaken in the first place given the presence of such extensive disease. RCC is not radio or chemo-sensitive so surgical excision is the only hope of cure. Several reviews have shown that in the absence of metastasis, complete excision of tumour thrombus together with radical nephrectomy may be associated with up to 72% survival at 5 years. Adverse prognostic factors for these patients are perinephric tumour...
extension and lymph node metastasis, which are similar to those in whom tumour thrombus is not present.

There are conflicting reports about the prognostic significance of the cephalad extent of tumour thrombus. A review of over one thousand patients demonstrated a statistically significant better overall survival in patients with thrombus in the RV compared to IVC involvement. Both were classified as pT3b tumours in previous TNM classifications. They have now been separated into different prognostic groups in the revised TNM classification. Other reviewers have shown that intra-atrial thrombus is not associated with a reduced survival when compared to lower levels of thrombus extension. On the other hand, invasion of the vascular endothelium by thrombus is associated with a poorer prognosis and increased morbidity since resection and reconstruction of the IVC is necessary in such cases.

Besides attempting to improve survival and alleviate symptoms when present, surgery in these cases is also aimed at minimising potentially fatal complications of IVC and intra-atrial thrombus including pulmonary embolism, peripheral oedema and atrial arrhythmias. We feel that this, coupled with the possibility of a curative resection, justifies the decision to offer surgery after very thorough pre-operative counselling of the patient.

Conclusion
Surgery for tumour thrombus extension in RCC may be associated with a good prognosis if no distant metastases are identified and if the thrombus can be completely excised. The surgical approach will depend on the cephalad extension of the thrombus, hence the importance of accurate pre-operative staging. When intra-atrial extension is present, CPB together with DHCA is an option that guarantees an optimal bloodless field while protecting vital organs. This provides the best opportunity for complete surgical excision of intra-atrial tumour thrombus that is crucial in optimising patient prognosis.

References