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Renal Cell Carcinoma with Vena Caval Thrombus Extending into the Right Atrium: Our Experience

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Abstract

Background and Aims: The incidence of inferior vena cava tumor thrombus is 4 – 10% in patients with renal cell carcinoma (RCC). Tumor thrombus may extend into the right atrium. Survival of patients with level IV tumor thrombus is believed to be poorer. Aim of the present study was to assess short term and long term survival in patients with level IV thrombus.

Methods: From July 1996 to March 2009, 7 patients underwent surgical treatment for localized RCC and inferior vena caval thrombus extending into the right atrium. All these patients underwent radical nephrectomy with inferior vena caval thrombectomy using cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest. Pathological investigations revealed no renal capsular penetration of RCC in 4 patients and perinephric fat involvement in 3.

Results: The mean operating time was 365 min (295-390), anaesthesia time was 395 min (335-440), cardiopulmonary bypass time was 128 min (38-200) and hypothermic circulatory arrest time was 28 min (14-38). The mean follow-up time was 38 months. Presence of capsular infiltration or positive lymph nodes significantly affected survival of patients in our study with no patient having a two year survival as opposed to 100% in patients with no capsular infiltration.

Conclusions: Long term survival following the surgical treatment is probable in individuals with localized RCC extending into the right atrium. Performance of complete radical nephrectomy along with vena caval thrombectomy under circulatory arrest is a safe procedure without significant morbidity. The management is evolving for this complex group of patients. A multidisciplinary approach is associated with good short and long term results.

Keywords: Renal Cell Carcinoma, Inferior Vena Cava, Heart Atrium

Introduction

One of the unique features of renal cell carcinoma (RCC) is its frequent pattern of growth intraluminally into the renal vein and further into the inferior vena cava (IVC). In extreme cases, this growth may extend as far as the right atrium. Involvement of the IVC with RCC occurs in 4% to 10% of patients (1). The absence of metastases in many patients with vena caval extension is an intriguing aspect of this cancer's behaviour (2). Approximately 45% to 70%

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of patients (1). The absence of metastases in many patients with vena caval extension is an intriguing aspect of this cancer's behaviour (2). Approximately 45% to 70% of patients with RCC and IVC thrombus can be cured with an aggressive surgical approach including radical nephrectomy and IVC thrombectomy (1). The staging of IVC thrombus is done depending on the level of the thrombus: I, adjacent to the ostium of the renal vein; II, extending up to the lower aspect of the liver; III, involving the intrahepatic portion of the IVC but below the diaphragm; and IV, extending above the diaphragm. The prognostic significance of the cephalad extent of the IVC thrombus has been controversial. Most studies suggest that the incidence of locoregional or systemic progression is higher in patients with level III-IV IVC thrombus, and this probably accounts for the reduced survival reported in this subgroup in some series (3-7). However, other reports confirm that many patients with level IV IVC thrombi can be cured of the disease with surgical resection, as long as the tumor is otherwise confined (8-10). We report our experience in the management of level IV IVC thrombus extending into the right atrium.

Materials and Methods

From July 1996 to March 2009, 10 patients presented us with non-metastatic RCC and an IVC thrombus extending into right atrium. Of these, 7 patients (6 males and 1 female), 32 to 65 years old underwent radical nephrectomy with extraction of IVC thrombus. RCC involved the right and left kidneys in 4 and 3 patients respectively. Every patient was subjected to a preoperative chest x-ray, bone scan and CT of the KUB (Kidney, Ureter and Bladder) region, to verify absence of gross lymph node involvement or metastatic disease. (Figures 1-3)

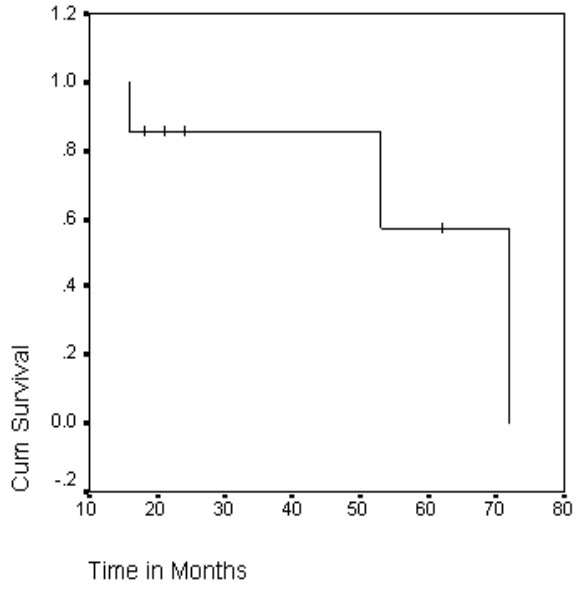

Figure 1. Kaplan-Meier cumulative survival of patients with RCC and level IV IVC thrombus

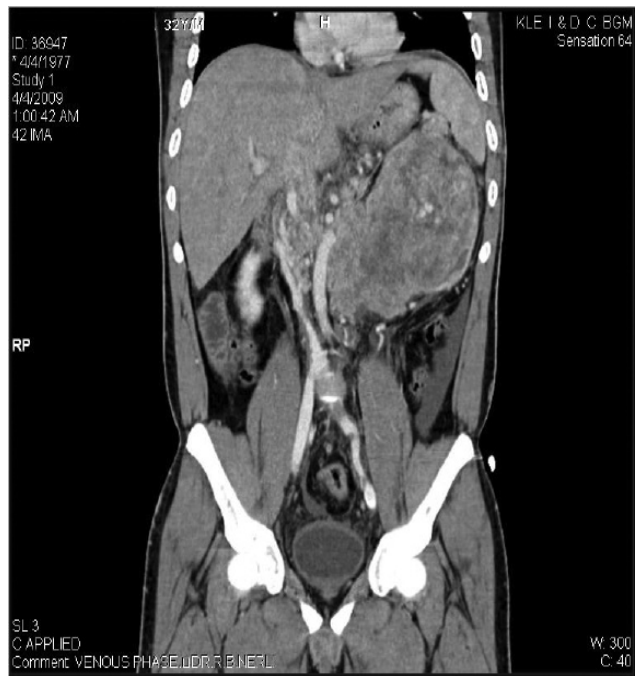

Figure 2. CT Scan Images showing a large tumor arising from and replacing whole of left kidney with tumor thrombus in the inferior venacava extending into the heart

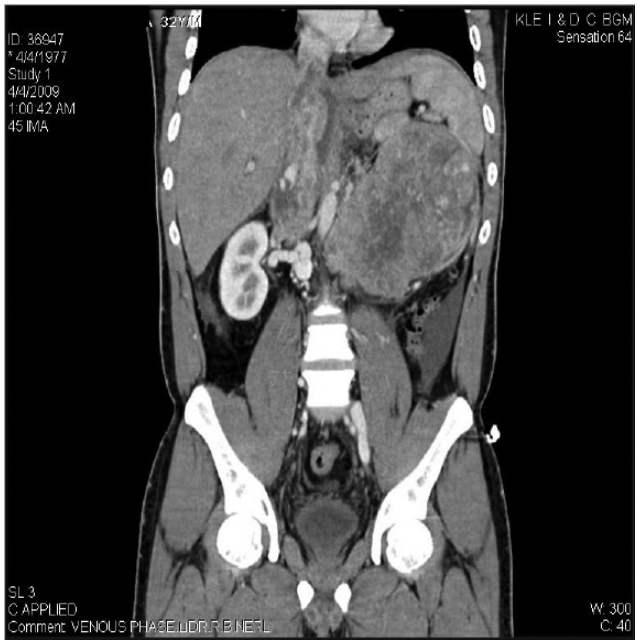

Figure 3. CT Scan Images showing a large tumor arising from and replacing whole of left kidney with tumor thrombus in the inferior venacava extending into the heart

Magnetic resonance imaging was done in 3 patients to determine the exact cephalad extent of the inferior vena cava thrombus. An echocardiogram was performed in all patients to confirm the presence of thrombus in the right atrium.

The abdomen was entered through a bilateral chevron incision and extended through a median sternotomy. The right colon and small bowel were mobilized along the white line of Toldt and small bowel mesentery, exposing the anterior surface of the inferior vena cava and both the renal veins.

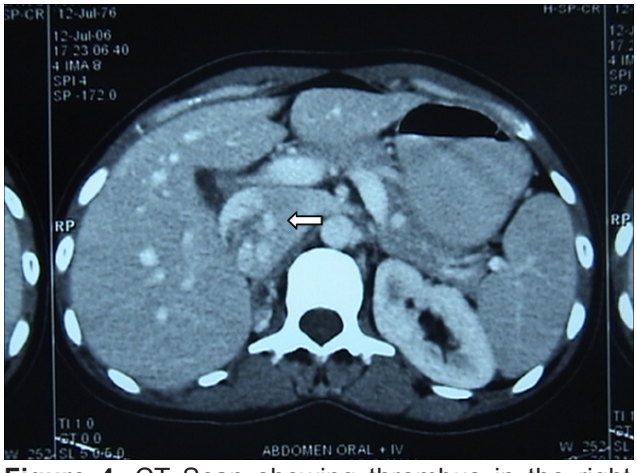

Figure 4. CT Scan showing thrombus in the right atrium

The involved kidney was dissected from all the sides and the renal artery was ligated. Once the tumour was dissected completely from all the sides, the patient was heparinised and cannulation was performed. The right atrium was cannulated with minimal handling and avoiding the tumour thrombus. A low profile 'Ross basket' cannula was inserted into the right atrial appendage. Cardiopulmonary bypass (CPB) was commenced and the patient was systematically cooled to a core temperature of 23 to 250 C. After the required temperature was attained, the patient was placed in Trendelenberg position. A separate atriotomy was made almost to the level of the diaphragm to allow complete visualization. The intra-abdominal IVC was simultaneously opened. The thrombus was gently manipulated and separated from the IVC, hepatic veins and right atrium (RA). The 'tumour waist' at the level of the diaphragm required careful manipulation to deliver the tumour tissue into the abdominal IVC. Another area of concern was the hepatic veins, which contained 'tongues' of tumour tissue and required exploration under vision via the RA to extricate. This was further aided by the use of Fogarty's embolectomy catheter. Nephrectomy along with thrombectomy was done. The cavotomy and atriotomy were then closed with continuous polypropylene sutures. Cardiopulmonary bypass was reversed, aortic clamp removed and the patient was rewarmed.

All of the patients were studied with a complete blood serum chemistry panel, chest x-ray and abdominal CT at 6 month intervals postoperatively. Bone scans were done whenever necessary. All hospital charts and follow-up information was obtained by contacting the patients and/or their attenders. Complete follow-up was available for all the patients. Cancer free status was determined by negative findings on the aforementioned studies. Survival analysis was calculated and the mean survival reflected the interval to last follow-up in patients still alive or to death.

Results

During the study period 10 patients with a mean age of 52.1 years presented with RCC and cavo-atrial extension. Of these, 7 underwent radical nephrectomy with complete removal of IVC thrombus. The remaining three declined to undergo surgery for financial reasons. One of the patients who declined surgery was also positive for HIV. Preoperatively, hepatic dysfunction was noted in two patients. The hepatic enzymes and serum bilirubin levels were raised. Three patients had elevated serum creatinine levels. All the patients were anaemic and two of these needed blood transfusions for preoperative workup. One of the patients had minimal ascites. Three patients had prominent veins in the lower half of the abdomen.

In all these patients, we preferred using cardiopulmonary bypass and instituted hypothermic circulatory arrest. The mean operative time was 365 min (range 295 – 390 min) and the mean anaesthesia time was 395 min (range 335 – 440 min). The mean cardiopulmonary bypass time was 128 min (range 38 – 200) and the mean hypothermic circulatory arrest time was 28 min (range 14 – 38). The mean intensive care and hospital stay was 2.5 and 14.5 days respectively. Two patients were re-explored within 8 hours for post-operative bleeding. The bleeding was noticed from the pericardium in one and the internal mammary vessels in the other. Post-operative blood transfusions were needed in three patients.

Histopathological study of the tumor revealed clear cell carcinoma in all. In 4 of these patients, further histopathological study revealed no renal capsular penetration of the tumor. Perinephric fat involvement was seen in two patients and hilar lymph nodes were positive for tumor in one. Of the 4 patients with no perinephric fat involvement, three were alive and one died at 62 months. Of the remaining three patients, two developed local recurrence at 8 and 9 months following surgery. One died at 16 months and the other has been on treatment with Sunitinib. One other patient died at 21 months due to brain metastasis.

The mean follow-up time was 38 months (range 16-72). The mean survival time was 58.6 months (Figure 5). There was significant difference in survival based on capsular penetration and positive lymph nodes. Presence of capsular infiltration or positive lymph nodes significantly affected survival of patients in our study with no patient having a two year survival as opposed to 100% in patients with no capsular infiltration.

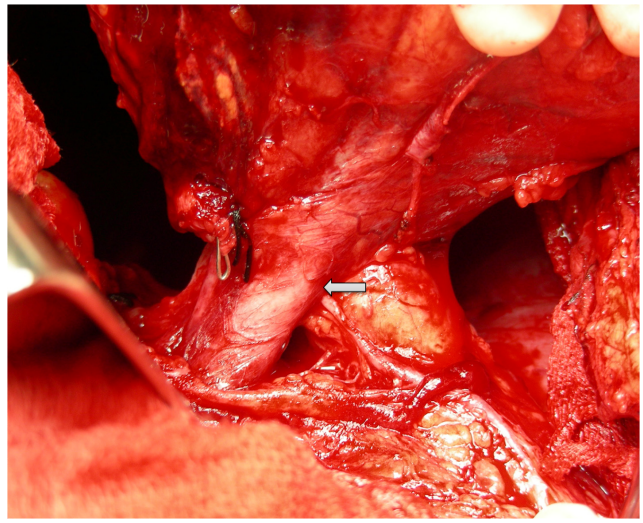

Figure 5. The renal mass being dissected all along with the renal vein showing thrombus extending in to the IVC

Discussion

Renal cell carcinoma extends into the IVC in 4 to 10% of all the patients (1). IVC involvement in RCC usually occurs by intraluminal extension of the tumour. It can if left untreated, lead to poor survival and quality of life. The 5 year survival rates of 47 to 68% have been reported following complete surgical excision of localized RCC in this setting (8, 9). Factors that finally influence the outcome in these patients include clinical staging, completeness of

resection, and biological characteristics of the primary tumor. Regional lymph adenopathy and distant metastasis are associated with poor survival. The prognostic significance of the cephalad extent of an inferior vena caval tumor thrombus with RCC is controversial. Suggestions have been made that survival following surgical treatment is diminished in patients with supra-diaphragmatic inferior vena caval involvement, even when there is no apparent metastatic disease at operation (3).

Although involvement of the IVC with RCC renders the task of complete surgical excision more complicated, operative removal offers the only realistic hope for cure in most of the patients (4, 11). After mobilization of the kidney and ligation and transection of the arterial blood supply, vascular control of the involved portion of the IVC is obtained. In general, level I thrombi are isolated by a Satinsky clamp and are thus readily removed. Level II thrombi require sequential clamping of the caudal IVC, contralateral renal vein and cephalad IVC along with mobilization of the relevant segment of the IVC and occlusion of lumbar veins. The renal ostium is then opened and the thrombus is removed, all in a bloodless field. On occasion, a tumor thrombus may locally invade the wall of the vena cava. Aggressive resection of the vena caval wall and attainment of negative surgical margins in these patients appear to provide a survival benefit (12). IVC grafting or reconstitution is required in some instances, but patients with a completely occluded IVC do not require it because of the collateral blood flow (13). Bland thrombus may be left in situ, although the cephalad IVC level should be occluded or clipped in this instance to prevent pulmonary embolism.

Vascular control for level III and level IV IVC thrombi requires more extensive dissection or cardiopulmonary bypass and hypothermic circulatory arrest. For level III thrombi, mobilization of the liver and exposure of the intra-hepatic IVC will often allow the thrombus to be mobilized proximal to the hepatic veins, and dissection can then proceed as for a level II thrombus (14). Level IV IVC thrombi have traditionally been managed with cardiopulmonary bypass and hypothermic circulatory arrest, and this is still the preferred approach in complex cases. Many centres are now trying to avoid hypothermic circulatory arrest and the associated hypocoagulable state that ensues after coming off the pump and the increased risk of cerebrovascular accident and myocardial infarction that accompanies this procedure (15, 16).

Blute et al (11) reported on the Mayo Clinic experience with the surgical management for patients with RCC and IVC thrombus. Assessment of 540 patients who underwent surgical resection for RCC with renal venous extension from 1970 and 2000 was made. Early and late surgical complications, including operative death, were compared with tumor thrombus level using the chi-square, Fisher's exact and Wilcoxon rank-sum tests. There were 349 (64.6%) patients with level 0 thrombus and 191 (35.4%) with inferior vena cava thrombus, including 66 (12.2%) with level I, 77 (14.3%) with level II, 28 (5.2%) with level III, and 20 (3.7%) with level IV thrombus. Patients with a higher thrombus level had more early surgical complications, though, there was no statistically significant variation in the incidence of late complications by thrombus level. The occurrence of any early surgical complication decreased from 13.4% for patients who underwent treatment in 1970-1989 to 8.1% for those treated in 1990-2000, the respective surgical operative mortality also decreased from 3.8% to 2.0% and in patients with inferior vena cava thrombus, from 8.1% to 3.8%. The respective duration of hospital stay decreased from a median of 8 to 7 days, however, the incidence of late complications increased significantly over time. There was a statistically significant variation in outcome for patients with level 0 v/s those with level >0 thrombus ($P = 0.002$, however, there was no significant difference in the outcome by thrombus

level among the patients with IVC tumor thrombus.

Ayati et al (17) reported on the outcome of 11 patients who had RCC with IVC tumor thrombosis. Four of these 11 had level IV thrombus with one extending into the right atrium. Four patients were tumor free (follow-up range 9 to 18 months) and 7 died due to multiple metastases during the follow-up. They concluded that extensive surgical treatment was the best means of treating these patients. Glazer and Novick (9) reported on their series of 18 patients who had RCC with IVC thrombus extending into the right atrium. All the patients underwent complete tumor excision with radical nephrectomy and IVC thrombectomy using adjunctive cardiopulmonary bypass and deep hypothermic circulatory arrest. Pathological study indicated no renal capsular penetration of RCC in 10 patients and involvement of perinephric fat in 8. The overall and cancer specific 5 year survival rates were 56.6% and 60.2%, respectively. Eight patients (45%) were free of malignancy at a mean of 71.6 months. Postoperatively, one patient survived for 15 months with metastatic disease. There was one operative death, while eight patients died of metastatic disease at a mean of 18.8 months postoperatively. Mean postoperative survival was significantly increased in patients with no renal capsular penetration when compared with those with perinephric fat association (58.1 vs 19.7 months, P=0.035). They concluded that long term survival after surgical treatment was possible in patients with localized RCC extending into the right atrium. In patients with localized RCC and IVC thrombus, the cephalad extent of the IVC involvement did not appear to be prognostically important.

Kalkat et al (18) reported on 68 consecutive patients who underwent surgical resection for RCC and IVC thrombus and required cardiothoracic surgical input. Of these, 21 patients required cardiopulmonary bypass (CPB). The overall two and five year survival rates were 50% and 37% respectively at a mean follow-up of 31 months. Cox regression suggested presence of metastasis and age > 70 years negatively affected the long term outcome. The level of tumour extension into the IVC did not have an important prognostic implication in their series. The patients with metastatic disease had relatively poor prognosis.

Our study has shown that patients with RCC and IVC thrombus extending into the right atrium can be offered surgical excision with minimal morbidity. The level of thrombus does not affect the outcome in these patients; however, the presence of Perinephric infiltration or positive lymph nodes significantly affects the survival.

Conclusions

Our series demonstrates that meticulous preoperative planning, intraoperative monitoring, surgical technique and prudent use of CPB and HCA is associated with good short and long term outcome in this complex group of patients with RCC extending into the right atrium. Extended cancer free survival is possible following surgical treatment.

Conflict of Interest

There is no conflict of interest to say regarding the article or financial support among the authors.

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