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The Role of Liver Transplantation Techniques in the Surgical Management of Advanced Renal Urothelial Carcinoma with or without Inferior Vena Cava Thrombus

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ABSTRACT

Purpose: Standard radical nephrectomy for large masses is significantly facilitated by liver transplantation techniques, which have been successfully employed over the last ten years at our institution. Large and locally-advanced urothelial carcinoma of the kidney with or without extension into the inferior vena cava is rare. The purpose of this study was to present the surgical management of large and locally-advanced urothelial tumors arising from the renal pelvis using liver transplantation techniques and to evaluate patient outcome.
Materials and Methods: Diagnostic work-up and surgical management of 4 patients with large and locally-advanced renal urothelial carcinoma were retrospectively reviewed. Two out of four patients with urothelial carcinoma presented with inferior vena cava thrombus. Mean tumor size was 11.6 cm. All patients underwent surgery, 2 patients with the presumed diagnosis of renal cell cancer. Liver transplantation techniques were an integral part in all radical nephrectomies.
Results: No intraoperative complications and postoperative mortality occurred. Mean operative time was 7.5 hours, estimated blood loss was 1.5 L, and an average of 4.8 units of blood was transfused intraoperatively. Three patients succumbed to cancer recurrence at a mean postoperative time of 6.3 months; 1 patient is still alive 24 months after surgery.
Conclusions: Large and locally-advanced renal masses of urothelial origin can be successfully removed by a combination of radical nephrectomy with liver transplantation techniques. Since long-term outcome of such patients has been poor, accurate preoperative diagnosis is essential to consider neoadjuvant treatment and to plan nephroureterectomy.

Key words: *urothelial carcinoma; kidney, nephrectomy; liver transplantation*
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INTRODUCTION

Urothelial carcinoma (UC) of the renal pelvis represents approximately 10% of all primary renal malignancies and its prognosis correlates with histological grade and stage (1,2). Advanced disease stages, such as invasion into renal parenchyma or perirenal fat with or without tumor extension into the inferior vena cava (IVC) carry a poor prognosis (3). IVC involvement is rare with only a few cases reported in the literature (4). Extirpation of these large renal masses poses a particular challenge to the urologic surgeon because adequate surgical exposure and subsequent nephrectomy rely on mobilization of adjacent organs such as liver and spleen. In cases of tumor extension into the IVC, additional exposure of the retrohepatic and suprahepatic IVC is necessary. Locally-advanced renal cell carcinomas (RCC) have been safely and completely removed by combining radical nephrectomy with surgical techniques derived

from liver transplantation over the last ten years at our institution (5).

The purpose of this study was to present the surgical management of large and locally-advanced urothelial tumors arising from the renal pelvis employing liver transplantation techniques and to evaluate patient outcome.

MATERIALS AND METHODS

Four patients with locally-advanced UC of the renal pelvis (≥ T3), two with extension into the IVC, were treated at our institution between 2003 and 2005. Pertinent preoperative work-up (imaging, laboratory), tumor characteristics (grade, stage), surgical approach, perioperative management, and patient outcome were reviewed. All four patients underwent standard preoperative evaluation including abdominal CT scans, chest X-rays or chest CT scans, and liver function tests. Bone scans and abdominal MRIs were obtained in 2 patients. Tumor thrombus extent was staged according to the Mayo Foundation classification (6). Cystoscopy and cytology were performed in 1 of 3 patients with a history of hematuria.

Liver transplantation techniques, in combination with nephrectomy for large and locally-invasive renal masses, have been previously described in detail (5). In brief, a bilateral subcostal incision, with superior midline T-extension is performed and a Rochard self-retaining retractor placed. This tri-radiate incision permits access to the liver, diaphragm, hepatic veins, and suprahepatic IVC and is the favored approach for orthotopic liver transplantation. Liver and IVC are mobilized in piggyback fashion. Liver mobilization begins with dissection, ligation and division of the ligamentum teres. The falciform ligament is then divided by cautery. This incision is carried around each portion of the divided falciform ligament to the right superior coronary ligament and divides the left triangular ligament. The visceral peritoneum on the right side of the hepatic hilum and the infrahepatic IVC are incised with the right inferior coronary and hepatorenal ligaments. At this stage, nephrectomy of most bulky masses can be safely carried out, however, in cases of IVC involvement, mobilization continues. The liver is gradually rolled to the left using the same techniques as in liver transplantation. In this fashion, the infrahepatic, intrahepatic, and suprahepatic portions of the IVC are completely exposed. The three hepatic veins are identified, their orifices inspected, and tumor removed. Following the removal of the tumor thrombus and IVC, the clamp is repositioned below the hepatic veins thus permitting continued hepatic venous drainage during the removal of the IVC and tumor thrombus. Exposure of the left kidney begins by mobilization of the descending colon. The spleen is dissected off the diaphragm and mobilized en bloc with the pancreas toward the midline. To gain access to the upper pole of the left kidney the left liver lobe is mobilized. The study was approved by the Institutional Review Board.

RESULTS

Three male and one female patient underwent surgery for large but clinically localized UCs of the renal pelvis; mean age was 65 years (range 59-74). Preoperative diagnosis was UC in 2 cases: One patient had undergone radical cystectomy with ileal conduit 6 years earlier suggesting upper tract UC; another patient underwent cystoscopy showing tumor protruding from the ureteral orifice. The remaining two patients with IVC thrombus entered surgery with the presumed diagnosis of RCC.

A bilateral subcostal incision with midline T-extension was the surgical approach in all 4 cases. Mean operative time was 7.5 hours, mean estimated blood loss was 1.5 L, and an average of 4.8 units of blood was transfused. Three nephrectomy specimens were bivalved in the operating room, which changed the diagnosis in one case and ureterectomy was consequently performed; the remaining specimen was not bivalved and the ipsilateral ureter was left in situ. Gross examination of the specimens demonstrated UC arising from the renal pelvis and invasion of the proximal ureter. None of the patients required cardiopulmonary bypass. There was neither an intraoperative complication nor an operative mortality. Postoperative morbidity occurred in 2 patients secondary to pulmonary embolism on postoperative day 2 and 61. Three patients underwent adjuvant chemotherapy; one could not proceed because of low

performance status. Three patients expired of disease recurrence at a mean of 6.3 months after surgery; one patient is alive without evidence of disease 24 months later (Table-1). All 4 patients were diagnosed with high-grade urothelial carcinoma arising from the renal pelvis. Tumor characteristics are shown in Table-2. Mean tumor size was 11.6 cm. In 2 patients the tumor extended into the IVC and in 2 patients lymph nodes were involved.

COMMENTS

To our knowledge this is the first study describing the application of liver transplantation techniques for the resection of large UCs of the kidney with and without IVC thrombus. The surgical technique described herein allowed excellent exposure and safe removal of the tumor in all 4 patients (5). Liver transplantation techniques proved essential for the resection of IVC thrombi in 2 patients and significantly improved exposure to the retroperitoneum allowing complete removal of the remaining two renal masses with a mean size of 12 cm. Albeit RCC of such size is amenable to conventional nephrectomy, UC of the renal pelvis is known to induce significant perirenal inflammation and desmoplastic reaction and is frequently associated with lymph node metastasis (7). Secondary to these adverse tumor characteristics operative time was considerably prolonged with a mean of 7.5 hours. No intraoperative complications or postoperative mortality occurred. In a series of 3 patients with renal UC and IVC thrombus, a midline approach was selected in 2 patients (one surgery was aborted due to extensive liver involvement) and an extended subcostal incision in the third. One of these patients was without evidence of disease 9 months after surgery, two died of respiratory failure within 2 months postoperatively (8).

Prognosis for upper tract UC, stage for stage, is reportedly inferior to that of bladder UC. While 5 year overall survival rates for stage T2, T3, and T4

Table 1 – *Treatment and outcome of patients with advanced urothelial carcinoma of the renal pelvis.*

Patient	EBL (mL)	Blood Transfusions	Operative Time	Morbidity	Adjuvant Chemotherapy	Recurrence	Survival
1	3000	11	7.6 hours	PE day 2	Cisplatin/Gemcitabine	Local	8 months
2	2000	5	8.3 hours		Cisplatin/Gemcitabine		Alive at 24 months
3	650	1	8.5 hours	PE day 61		Local	2 months
4	500	2	5.7 hours		MVAC	Metastatic	10 months

EBL = estimated blood loss; PE = pulmonary embolism; MVAC = methotrexate, vinblastine, doxorubicin, cisplatin.

Table 2 – *Tumor characteristics. High-grade urothelial carcinoma of the renal pelvis was the diagnosis in all cases.*

Patient	Side	Margins	Tumor Size (cm)	Inferior Vena Cava Thrombus	TNM Stage	Positive Lymph Nodes
1	Right	Negative	8 x 6 x 6	Retrohepatic below hepatic veins	T3 N0 Mx	0
2	Left	Positive	11 x 6 x 5.5		T3 N0 Mx	0
3	Right	Positive	15.4 x 10.2 x 8	Infrahepatic	T4 N2 Mx	6
4	Right	Negative	12 x 5 x 4		T3 N2 Mx	2

bladder UC are 72%, 40%, and 33%, they are 60%, 15% and 15% for upper tract UC (3,9). Neoadjuvant chemotherapy for patients with ≥ T2 bladder UC in prospective randomized clinical trials has demonstrated survival benefits (10,11). However, there is no evidence supporting neoadjuvant chemotherapy for upper tract UC. None of our patients received neoadjuvant chemotherapy; however, we speculate that it may have improved patient survival as previously demonstrated for bladder UC (intact vasculature, improved resectability, early control of occult metastases, better performance status). Neoadjuvant chemotherapy may furthermore result in better outcome than adjuvant chemotherapy because many patients do not receive optimal dosing of systemic chemotherapy after nephrectomy (12). One out of four patients with UC in our series was unable to commence adjuvant chemotherapy because of low performance status. Despite complete tumor resection, 3 out of 4 patients died of disease recurrence within 10 months after surgery, of whom 2 had undergone adjuvant chemotherapy.

Consideration of neoadjuvant chemotherapy relies on correct preoperative diagnosis. Two out of four patients in this study entered surgery with the presumptive diagnosis of RCC. Despite the presence of hematuria in 3 out of 4 patients, only 1 underwent cystoscopy, which established the correct diagnosis. Therefore, the finding of a large renal mass with or without IVC thrombus in patients with history of hematuria requires a complete hematuria work-up (13). According to the literature only 30% of patients with upper tract UC underwent surgery with the correct preoperative diagnosis. Several factors may contribute to the fact that large renal UC is frequently mistaken for RCC preoperatively (4). 1. UC arising from the renal pelvis is uncommon with an incidence of 7% to 15% of all primary renal malignancies (1,2). 2. RCC represents 85% of all primary renal malignancies and extends into the IVC in 4-10% (14,15). 3. A significant history of cigarette smoking and hematuria exists for both RCC and UC. 4. While upper tract UC presents with non-specific findings on imaging studies, CT scan may be a useful tool to differentiate renal UC from RCC (4,16). 5. IVC thrombus formation of UC is exceedingly rare with 21 cases reported in the literature (4). Meta-analyses evaluating the management of UC with IVC extension showed that in approximately 30% of patients a preoperative MRI was obtained. Only 20% had a positive cytology and all patients, in whom a retrograde pyelography was performed, demonstrated a renal pelvic/ureteral filling defect. In 60% of cases, nephrectomy without ureterectomy was performed and average survival was 6 months (17,18). Renal UC has a propensity to recur in the ipsilateral ureter at a rate of 30 to 40% and mandates radical nephroureterectomy (19,20). In one of our patients, with the presumed diagnosis of RCC, the ureter was left in situ.

CONCLUSIONS

Large and locally-advanced urothelial carcinomas of the renal pelvis can be successfully removed by enhancing standard radical nephrectomy with liver transplantation techniques; however, survival is poor. Preoperative diagnosis of renal urothelial carcinoma requires a high index of suspicion and is essential to consider neoadjuvant treatment and to plan nephroureterectomy.

CONFLICT OF INTEREST

None declared.

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