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## Upper Urothelial Tract Carcinoma: Case Series from Tertiary Oncological Care Centre and Review of Literature

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**Abstract**

**Introduction:** Urothelial carcinoma is the fourth most common solid malignancy<sup>1</sup> in the world. The majority (90–95%) of cases occur in the lower urinary tract (urinary bladder and urethra) and the rest in the upper urinary tract (renal calyces, renal pelvis, and ureter).<sup>2</sup> The management of Upper urothelial malignancy is nephroureterectomy with bladder cuff excision. This Case series reviewed the patients treated in a tertiary care and analyzed systematically regarding management. **Case series:** Upperurothelial tract carcinoma (UUTC) admitted and operated at government Royapettah hospital, Chennai, Tamilnadu for the past 4 years were taken and reviewed. There were 4 cases were operated in our hospital. Average age at diagnosis was 50.6 yrs. All four patients were males. All patients were evaluated by contrast enhanced CT scan. Cystoscopy done routinely for all cases and found no synchronous bladder cancer. All patients underwent laparoscopic assisted nephroureterectomy with open resection of distal ureter with bladder cuff margin. Among these one patient had microscopic margin positive at bladder cuff and treated with radiation. **Discussion:** Renal pelvis UTUCs are twice as common as those found in the ureter.<sup>4</sup> In terms of staging, 60% of UTUCs are invasive ( $\geq$ pT2) at diagnosis in contrast to the 15–25% for bladder cancers.<sup>5</sup> About 7% of patients present with metastatic disease.<sup>6</sup> Regarding imaging CT urogram has become the standard of care. The gold standard of treatment for patients with upper tract urothelial neoplasms and a normal contralateral kidney is complete nephroureterectomy with removal of a cuff of urinary bladder. A retroperitoneal lymph node dissection along the ipsilateral great is performed for more complete surgical staging, especially for higher grade and invasive cancers. A lymphadenectomy may not be necessary in cases of UTUC which are low stage and low grade. In our case series, Average operating time was 142 min. Average blood loss was 240 ml. All patients had decreased analgesia frequency (mean 2.1 days), faster return to ambulation (mean 1.5 days), with mean hospital stay of 8 days. In our institute we resected the distal ureter with bladder cuff excision by open technique. **Conclusion:** In summary, laparoscopic nephroureterectomy with open bladder cuff excision was a safe and acceptable alternative to open nephroureterectomy with bladder cuff excision. Cancer control rates seem to be similar with superior convalescence, but need follow up and large no of cases to mention about recurrence. In terms of managing the distal ureter and bladder cuff, the open technique is the most efficacious in terms of achieving negative margins and decreased risk of cancer seeding.

**Keywords:** Upper urothelial tract carcinoma; Nephroureterectomy with bladder cuff removal.

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**Introduction**

Urothelial carcinoma is the fourth most common solid malignancy<sup>1</sup> in the world. The majority (90–95%) of cases occur in the lower urinary tract (urinary bladder and urethra) and the rest in the

upper urinary tract (renal calyces, renal pelvis, and ureter).<sup>2</sup> The management of Upper urothelialtract carcinoma (UUTC) is nephroureterectomy with bladder cuff excision. This Case series reviewed the patients treated in a tertiary care and analyzed systematically regarding management.

## Case series

### Case Capsule 1

A 65 years old male patient, presented with complaints of painless terminal hematuria for past 1 month. On examination there was a no mass felt per abdomen. Urine cytology studies revealed urothelial cells on microscopic examination. CT urography imaging revealed left renal pelvis tumor of size 2\*3 cm extending into upper ureter. Patient underwent laparoscopic assisted left nephroureterectomy with open bladder cuff removal. Post operative period was uneventful. Post operative histopathology showed low grade urothelial carcinoma pT1N0.

### Case Capsule 2

A 56 years old male patient, presented with complaints of right loin pain for past 1 month. On examination there was a right lumbar mass which was ballotable. CT urography imaging revealed right renal pelvis tumor of size 4\*4 cm. Patient underwent laparoscopic assisted right nephroureterectomy with open bladder cuff removal. Post operative period was uneventful. Post operative histopathology showed low grade urothelial carcinoma pT2N0.

### Case Capsule 3

A 68 years old male patient, admitted with complaints of painless terminal hematuria for past 1 year. On examination there was a ballotable right lumbar mass. Urine cytology studies revealed malignant urothelial cells on microscopic examination, suggestive of urothelial carcinoma. CT urography imaging revealed left renal pelvis tumor of size 5\*3 cm. Patient underwent laparoscopic assisted left nephroureterectomy with open bladder cuff removal. Post operative period was uneventful. Post operative histopathology showed low grade urothelial carcinoma pT3N1, and microscopic margin positive at resected bladder cuff. Patient was discussed in tumor board and subjected for adjuvant chemotherapy.

### Case Capsule 4

A 56 years old male patient, presented with complaints of right loin pain for past 1 month. On examination there was no significant abnormality. CT urography imaging revealed right renal pelvis tumor of size 2\*2 cm. Patient underwent laparoscopic assisted right nephroureterectomy with bladder cuff removal. Post operative period was uneventful. Post operative histopathology showed high grade urothelial carcinoma pT2N0.

Average age at diagnosis was 50.6 yrs. All four patients were males. All patients were evaluated by contrast enhanced CT scan. Cystoscopy done

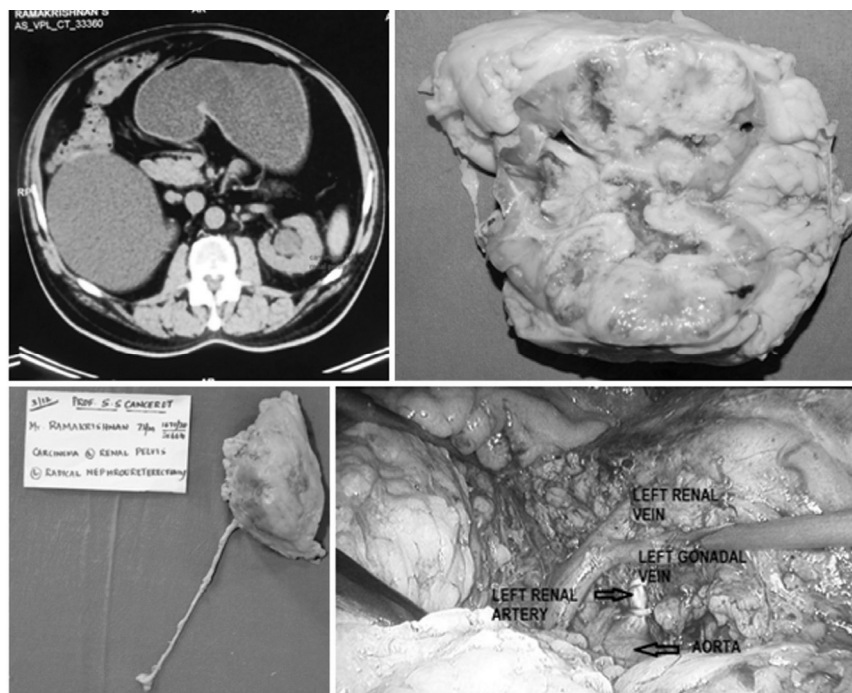


Fig. 1.

routinely for all cases and found no synchronous bladder cancer. All patients underwent laparoscopic assisted nephroureterectomy with open resection of distal ureter with bladder cuff margin.

**Laparoscopic radical nephrectomy** is done medial to lateral through a transperitoneal approach.

10-mm umbilical, camera port, 10-mm right hand working port in the epigastrium pararectally, 5-mm left hand working port at the level of umbilicus for right side nephrectomy and for left side tumors 10 mm working port at the level of umbilicus on left side one hand breadth aside from umbilical port and 5 mm working port epigastrium pararectally. Retraction port as per the need placed in the subcoastal or epigastrium.

- *Kocherization* The duodenum is kocherised until the IVC is clearly visualized. On the left side colonic mobilisation is done medially along with division of lenorenal and phrenocolic fascia. Further mobilisation is possible with retraction of tail of pancreas
- *Reflection of the colon:* Along the white line of Toldt, the right colon or left colon is reflected medially across the midline to provide an adequate visualization of the anterior surface of Gerota's fascia.
- *Securing the renal blood vessels:* The retraction of the liver to improve the visualization of the right renal hilum is done. The dissection of the right renal vein in relation to IVC is done by using the Harmonic scalpel. On left side spleen and pancreatic tail was reflected medially and accessed the renal vessels. The right renal artery which lies inferior and posterior to the right renal vein is dissected and clipped with two hemoclips proximally and with one distally. The renal artery is divided first to prevent congestion of the kidney. The adrenal vein is clipped and divided. All fibro fatty tissues with lymph nodes around the renal hilum are dissected upward toward the specimen. In the same way for left side also renal artery divided between hemoclips. These separation of the kidney from the lateral abdominal wall is done at last so that the specimen does not fall on the operative field.
- *Dissection of the ureter:* The psoas tendon is a reliable landmark when searching for the gonadal vein and ureter. Once located, the ureter is elevated from the psoas muscle and clipped.

- *Open distal ureteric resection with bladder cuff excision:* With Inguinal skin crease (small muscle-splitting incision in the ipsilateral iliac fossa made. Distal ureter mobilised and bladed cuff excision done. Specimen removed along with a cuff of bladder. Bladder defect closed with vicry in two layers.

In our case series, Average operating time was 142 min. Average blood loss was 240 ml. All patients had decreased analgesia frequency (mean 2.1 days), faster return to ambulation (mean 1.5 days), with mean hospital stay of 8 days. Post operatively one patient had microscopic distal ureteric margin positivity, was treated with adjuvant Radiation. All patients are in regular follow up and disease free until now (last case- 14 months).

## Discussion

### *Epidemiological Factors*

The estimated annual incidence in Western countries is about 2 per 100,000 inhabitants.<sup>2</sup> UTUC is three times more common in men than women and has a peak incidence in the age 70-90 yr.<sup>1,3</sup> Renal pelvis UTUCs are twice as common as those found in the ureter.<sup>4</sup> In terms of staging, 60% of UTUCs are invasive ( $\geq$ pT2) at diagnosis in contrast to the 15-25% for bladder cancers.<sup>5</sup> About 7% of patients present with metastatic disease.<sup>6</sup> Risk factors associated with UTUC are similar to urothelial bladder cancers such as cigarette smoking and various occupational exposures to carcinogenic aromatic amines including benzidine and beta-naphthalene.<sup>2,7</sup>

*Arsenic:* Unusually high incidences of upper urinary tract tumors have been reported in Blackfoot disease-endemic areas in the southwest coastal region of Taiwan, and the arsenic contaminated water has been postulated to be the cause of this prevalence and 1:2 female incidence is caused by arsenic fumes during cooking.<sup>16,17,19</sup>

Balkan endemic nephropathy and Chinese herb nephropathy are similar diseases related to UTUC.<sup>8</sup> It is believed to be due to dietary exposure to aristolochic acid. Aristolochic acid is derived from Aristolochic plants (fangchi and clematis).<sup>9,10,11</sup>

Lynch syndrome or hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal dominant genetic disorder that impairs DNA mismatch repair. According to Koornstra et al,

patients with HNPCC have 22-fold increased relative risk of developing UTUC.<sup>12</sup>

### *Imaging*

Historically, intravenous urography was the mainstay of a radiographic evaluation of upper tract tumors, but for the past several years, CT urogram has become the standard of care.<sup>24</sup> An MRI urography may also be useful in patients when sensitivity to iodinated contrast prevents the use of that agent.<sup>25</sup> We took CT urography in all 4 patients.

### *Management*

The gold standard of treatment for patients with upper tract urothelial neoplasms and a normal contralateral kidney is complete nephroureterectomy with removal of a cuff of urinary bladder. A retroperitoneal lymph node dissection along the ipsilateral great vessel (the vena cava for right-sided tumors; the aorta for left-sided tumors) for a renal pelvic and/or ureteral tumor above the iliac vessels, or an ipsilateral pelvic lymph node dissection for a distal ureteral tumor is performed for more complete surgical staging, especially for higher grade and invasive cancers. A lymphadenectomy may not be necessary in cases of UTUC which are low stage and low grade.

### *Nephroureterectomy*

Surgery can be done either open or laparoscopically. In our centre we did with laparoscopic assisted nephroureterectomy and bladder cuff excision.

Hall and colleagues<sup>13</sup> reported in one of the largest series in the literature on 252 patients who were treated for upper tract urothelial tumors with a median follow-up of 64 months. Patients undergoing parenchymal-sparing surgery had a lower actuarial 5-year disease-free survival rate than those treated with initial aggressive surgical resection (23% vs 45%, P\_.0009). This study supported the use of aggressive open surgical resection for initial treatment of upper tract urothelial tumors, with a 5-year disease-free survival rate of 45%.

Transperitoneal laparoscopic nephroureterectomy has had similar successes, as seen in the literature.<sup>23,24</sup> Advantages to a transperitoneal approach compared with a retroperitoneal approach include a familiarity with anatomic landmarks and a larger working space. The retroperitoneal approach, however, has

distinct advantages, including early control of the renal artery and vein, no manipulation of the bowel leading to less incidence of ileus and possibly a shorter hospital stay, and confinement of possible urinomas or seromas to the retroperitoneal space.<sup>13</sup>

The first laparoscopic nephroureterectomy was performed by Clayman in May 1991 at Washington University (St. Louis, MO), numerous reports have been published regarding the safety and efficacy of this procedure.<sup>14-23</sup> Blood loss was significantly less in the laparoscopic group (242 vs 696 mL). Postoperatively, patients in the laparoscopic group had a significantly more rapid resumption of ambulation (1.4 vs 2.5 days), oral intake (1.6 vs 3.2 days), shorter hospital stay (2.3 vs 6.6 days), decreased analgesic requirements (26 mg morphine sulfate equivalent vs 228 mg), and a quicker convalescence (8 vs 14.1 weeks).

In our case series, Average operating time was 142 min. Average blood loss was 240 ml. All patients had decreased analgesia frequency (mean 2.1 days), faster return to ambulation (mean 1.5 days), with mean hospital stay of 8 days.

Patients in the hand-assisted group had a similar operative time (233 vs 236 minutes), decreased blood loss (236 vs 427 mL), decreased analgesia frequency (2.1 vs 4.1 days), faster return to ambulation (1.5 vs 2.5 days), and shorter hospital stay (13 vs 21.1 days).

## **Management of Distal Ureter and Bladder Cuff**

### *Techniques include*

- 1) open excision
- 2) transvesical laparoscopic detachment and ligation technique
- 3) laparoscopic stapling of the distal ureter and bladder cuff
- 4) the "pluck" technique.

An open technique involves initial dissection of the renal unit laparoscopically. Once this is completed, the ureter is clipped but not ligated to prevent potential downstream seeding of tumor cells. The distal ureter is identified and dissected toward the bladder. The specimen is then removed en bloc with a rim of bladder cuff. The bladder may either be opened and the ureter dissected intravesically and extravesically, or the bladder may be spared and the full dissection performed

extravesically.

In our institute we resected the distal ureter with bladder cuff excision by open technique.

## Conclusion

In summary, laparoscopic nephroureterectomy with open bladder cuff excision was a safe and acceptable alternative to open nephroureterectomy with bladder cuff excision. Cancer control rates seem to be similar with superior convalescence, but need follow up and large no of cases to mention about recurrence. In terms of managing the distal ureter and bladder cuff, the open technique is the most efficacious in terms of achieving negative margins and decreased risk of cancer seeding. In order to avoid microscopic or macroscopic margin positive, intra-operative frozen section of bladder cuff may be advocated.

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