

Outcomes of Upper Urinary Tract Urothelial Carcinoma with Different Treatment Modalities: A Case Series from a Tertiary Care Centre

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Abstract:

INTRODUCTION: Arising from the urothelial lining of the urinary tract from the renal calyces to the ureteral orifice, the incidence of upper tract urothelial carcinoma (UTUC) has been increasing over the past 2 decades. UTUC currently comprises 10% of all renal tumors and 5% of urothelial malignancies overall. The clinico-epidemiological profile of this disease have been extensively studied in many countries, data regarding this in West Bengal is limited.

AIMS: To describe the clinico-epidemiological characteristics of upper tract urothelial carcinoma and its primary treatment modalities in a single tertiary care centre.

MATERIALS AND METHODS: Data were collected retrospectively from patients diagnosed with upper tract urothelial carcinoma and managed in urology department of Nil Ratan Sircar Medical College, Kolkata, from June 2016 to June 2019 (n=10). The indication for radical nephroureterectomy (RNU) was the presence of upper urinary tract transitional cell carcinoma in the absence of systemic metastatic disease. Our patient population underwent RNU by multiple surgeons, likely representing a significant case selection bias and variability of surgical techniques.

RESULTS: Pathologic examination revealed renal pelvic location (30%), ureteric location (60%), papillary growth (80%), necrosis (20%), lymphovascular invasion (LVI) (80%), concomitant carcinoma in situ (20%), and high-grade disease (100%). All except three patients (70%) in our series underwent open radical nephroureterectomy with excision of bladder cuff. In one of the patients in our series we had to perform an R2 resection because of involvement of IVC and iliac vessels (10%). Two patients in our series underwent organ sparing surgery (segmental resection and laser ablation). One received post operative chemoradiotherapy, the other had positive margins and underwent RNU. 7 out of the 9 patients operated at our centre had complete resection, 6 of whom had T3 disease and received adjuvant chemoradiotherapy. One patient with T2 disease had lymphovascular invasion and received adjuvant chemoradiotherapy. One of the ten patients (10%) in our series presented with metastatic disease at the time of presentation. The median follow up in our study was 13 months. At the end of follow up, overall survival and disease-specific survival rates were 70% (07/10) and 80% (08/10), respectively. Among the 10 patients, 2 died of UTUC. We had no cases of recurrent UTUC. Two of the patients in our series presented with a bladder recurrence 1-1.5 years after radical nephroureterectomy.

CONCLUSION: The rarity of this disease precludes significant advances by a single institutional experience. A collaborative effort among institutions using uniform diagnostic and treatment protocols could accelerate treatment advances, particularly for high risk patients who succumb to the disease.

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I. Introduction

Arising from the urothelial lining of the urinary tract from the renal calyces to the ureteral orifice, the incidence of upper tract urothelial carcinoma (UTUC) has been increasing over the past 2 decades. UTUC currently comprises 10% of all renal tumors and 5% of urothelial malignancies overall^{1,2}. Radical nephroureterectomy (RNU) with excision of an ipsilateral bladder cuff, and retroperitoneal LN dissection is the gold-standard therapy for upper-tract cancers. A few patients with small, lowgrade lesions may be candidates for endoscopic tumor ablation or segmental resections. Several single-center series of patients treated with RNU for UTUC have been published.³⁻⁷ These reports have contributed to the current knowledge of the natural history and the prognostic factors important in UTUC but conclusions have been limited by small patient population as well as variation in the study populations, related to diagnosis, patient selection, staging, pathologic evaluation, and treatment. It has been established that a significant number of UTUC patients eventually die of their disease

due to unrecognized metastases present at the time of surgery, thereby requiring a thoughtful integration of adjuvant or neoadjuvant therapy strategies for high risk patients .

AIMS

To describe the clinico-epidemiological characteristics of upper tract urothelial carcinoma and its primary treatment modalities in a single tertiary care centre.

II. Material And Methods

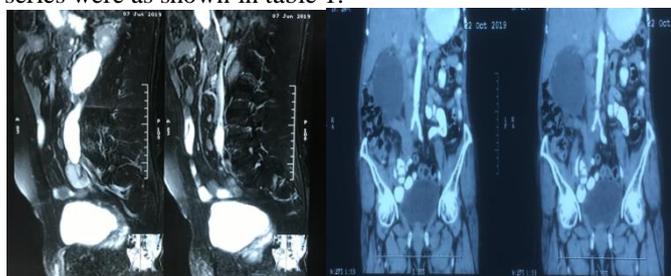
Data were collected retrospectively from patients diagnosed with upper tract urothelial carcinoma and managed in urology department of Nil RatanSircar Medical College, Kolkata, from June 2016 to June 2019 (n=10). The indication for RNU was the presence of upper urinary tract transitional cell carcinoma, in the absence of systemic metastatic disease. One of them had metastatic disease at the time of diagnosis and was subsequently referred for palliative chemoradiation. Two had associated comorbidities with poor performance status . One underwent segmental resection instead of radical surgery and the other underwent endoscopic laser ablation. Tumors staged according to the American Joint Committee on cancer Tumor-Node- Metastasis (TNM) classification.⁸ Tumor grading assessed according to the 1998 WHO/ISUP consensus classification.⁹ In addition, all specimens were evaluated for tumor location, pattern of tumor growth (papillary vs sessile), presence of LVI, tumor necrosis, and concomitant CIS. Follow-up was performed according to institutional protocols. Patients were generally followed every 3 months to 4 months for the first year following RNU, every 6 months from the second through the fifth year, and annually thereafter. Approval for the study was obtained from the Ethics and scientific Committee of the Institute.

III. Results

Diagnostic evaluation

The common presenting symptoms in our case series were as shown in table 1.

Table 1 . Symptoms	Percentage of patients
Hematuria(gross/microscopic)	90
Dysuria	20
Abdominal mass	30
Flank pain	50
Weight loss	10
Fatigue	30
Bone pain	0
Anorexia	30
Asymptomatic	10



While all the patients in our series had filling defects on CT urography films ,all except one patient had signs of obstruction. On cystoscopy two patients had synchronous bladder cancer in our series , involving the periureteric region. Cytology was positive for urothelial malignancy in two of the ten patients (20%) . They were later found to have high grade lesions on biopsy of the surgical specimen. We performed ureteroscopy in only one of our patients (10%) in whom the CT findings were inconclusive. We found an obvious luminal mass in that patient

Patient Characteristics

Patient characteristics were as described in table 2.

Table 2. Clinical Patient Characteristics		
Median age		69.7
Sex	Women	30%
	Men	70%
ECOG performance status (%)	0	70
	1	10
	≥2	20
Previous bladder urothelial carcinoma diagnosis (%)		0
Previous upper tract endoscopic therapy		0
Neoadjuvant systemic chemotherapy (%)		0
Adjuvant systemic chemotherapy (%)		9
Adjuvant external beam radiation (%)		8
Palliative chemoradiation		1

Table 3. Modality	Neoadjuvant therapy	Adjuvant chemoradiation	Surgery for recurrent disease	Mortality
Radical Nephroureterectomy(n=7)	None	All	TURBT for recurrent bladder sol	Two
Local tumour ablation(n=1)	None	Margins positive had to undergo RNU	None	-
Segmental resection(n=1)	None	Received	None	-
Palliative chemoradiation (n=1)	-	-	-	One

Treatment characteristics (Table 3)

All except three patients(70%) in our series underwent open radical nephroureterectomy with excision of bladder cuff. In one of the patients in our series we had to perform an R2 resection because of involvement of IVC and iliac vessels(10%). Two patients in our series underwent organ sparing surgery (segmental resection and laser ablation) . One received post operative chemoradiotherapy, the other had positive margins and underwent RNU. 7 out of the 9 patients operated at our centre had complete resection , 6 of whom had T3 disease and received adjuvant chemoradiotherapy

Pathologic Staging (Table 4)

Pathologic examination revealed renal pelvic location (30%), ureteric location(60%), papillary growth (80%) ,necrosis (20%), lymphovascular invasion (LVI) (80%), concomitant carcinoma in situ (20%), and high-grade disease (100%)

Table 4. Pathologic Tumor Characteristics		
pT stage (%)	T0	0
	Ta	0
	Tis	20
	T1	0
	T2	10
	T3	80
	T4	10
pN stage (%)	Unknown	8
	Negative	0
	Positive	1
Grade (%)	Low	0
	High	100
	Concomitant carcinoma in situ (%)	20
Index tumor location (%)	Renal pelvis	30
	Ureter	60
	upper	0
	middle	40
	lower	20
Tumor growth architecture (%)	Papillary	80
	Sessile	20
Lymphovascular invasion (%)		80
Tumor necrosis (%)		20

IV. Discussion

Upper urinary tract carcinoma at our centre they comprised 3.8 percent of the urothelial carcinoma in the past 2 years. Peak incidence at our centre occurred in individuals in their 70s and 80s. Most occurrences were in a single renal unit, and we had no synchronous bilateral urothelial upper tract tumours .Two of the patients in our series had synchronous upper tract and bladder tumour. We came across bladder tumours in two cases after RNU during the follow up period. One year survival rate at our centre was 70%. Among the mortalities one had metastatic disease and two had locally advanced regional disease. Pathologic examination revealed renal pelvic location (30%), ureteric location(60%), papillary growth (80%) ,necrosis (20%), lymphovascular invasion (LVI) (80%), concomitant carcinoma in situ (20%), and high-grade disease (100%). The role of LVI as a prognostic factor for progression and survival after RNU is controversial. Although several studies have identified LVI as a poor prognostic feature, only a few have controlled for possible confounding factors by using multivariate analyses.^{4,10,11,12,13} Only one patient (10%) had multifocal tumour involving the entire ureter and the renal pelvis. Several investigators have reported that the tumor growth pattern, an independent predictor of oncologic outcome in patients treated with radical cystectomy for urothelial carcinoma of the urinary bladder.^{14,15} The median follow up in our study was 13 months .At the end of follow up, overall survival and disease-specific survival rates were 70% (07/10) and 80% (08/10), respectively. Among the 10 patients, 2 died of UUTC. One patient had rapid metastases and died while receiving the palliative treatment. We had no cases of recurrent UUTC .Two of the patients in our series presented with a bladder recurrence 1-1.5 years after radical nephroureterectomy. Our patient population underwent RNU by multiple surgeons, likely representing a significant case selection bias and variability of surgical techniques.

V. Conclusion

The rarity of this disease prevents significant advances in management by a single institutional experience. A collaborative effort among institutions using similar diagnostic and treatment protocols could accelerate treatment advances, particularly for high risk patients who succumb to this rare disease.

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