

Non-transitional cell carcinoma of the upper urinary tract: A case series among 305 cases at a tertiary urology institute

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Abstract Non-transitional cell carcinomas (non-TCC) of the upper urinary tract as squamous cell carcinoma (SCC), adenocarcinoma, and small cell carcinoma (SmCC) are rare with few case reports in the literature. We retrospectively reviewed our patients who surgically treated for upper tract urothelial carcinoma from 1983 to 2013 for non-TCC pathological cancer characteristics and survival. Among 305 patients, only 5 (1.6%) cases were found: One case of SmCC, another had adenocarcinoma, and 3 SCC cases. None of them had intravesical recurrence and the cancer-specific survival for non-TCC cohort is markedly decreased (log-rank = 0.01) compared to TCC patients.

Key Words: Adenocarcinoma, kidney pelvis neoplasms, small cell carcinoma, squamous cell carcinoma, ureteral neoplasms, urologic neoplasms

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INTRODUCTION

Upper tract urothelial carcinoma (UTUC) arises from the urothelial lining of the urinary tract from the renal calyces to the ureteral orifice. They comprise 10% of all renal tumors and 5% of all urothelial malignancies.^[1] Transitional cell carcinomas (TCCs) are the most common primary tumor of UTUC. Although non-TCC such as squamous cell carcinoma (SCC), adenocarcinoma, small cell carcinoma (SmCC), and undifferentiated carcinomas are rare, but they exist. Chronic irritation and chronic infection of the upper tract are among the most common risk factors for the development of such rare tumors.^[2]

There are few case reports in the literature because of the rarity of the disease. Concurrently, there is a wide range of the incidence of non-TCC of the upper urinary tract (1.9–8%).^[3-5] Thus, subsequent more studies are needed from single institutions to narrow the true range of incidence.

Even in the urinary bladder (UB) carcinoma which comprises about 95% of urothelial tumors, there is also a paucity of data in non-TCCs of the bladder with only a few studies.^[6-8] The recommendations were for more case reporting to advance our understanding of these tumors and for a universal treatment algorithm.

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We are showing non-TCC pathological features in detail, cancer characteristics, and survival among more than 300 UTUC.

MATERIALS AND METHODS

After Institutional Review Board approval, we retrospectively reviewed our ongoing database for patients who were surgically treated for UTUC from 1983 to 2013. Patients with non-TCC at the final histopathology were selected for review.

Most of the patients were treated by standard radical open/laparoscopic nephroureterectomy with bladder cuff excision procedures. Renal-sparing surgeries were done in a few cases.

Surgical specimens were processed according to the standard pathological procedure. The tumor was staged according to the 1997 TNM classification, and the most traditional 3-tiered WHO grading system was used for pathological grading by different pathologists.^[8] None of our patients received neoadjuvant or adjuvant chemotherapy.

The postoperative regimen in the first 2 years included a cystoscopy every 3 months and contrast-enhanced computed tomography (CT) every 6 months. From the 3rd to 5th year, a cystoscopy every 6 months and a CT annually; thereafter, clinical examination, urine analysis, and cytology were ordered annually. Frequency and percentage were used for categorical variables. Cancer-specific survival was estimated using Kaplan–Meier methods.

CASES

Squamous and/or glandular differentiation was reported with TCC in 33 (10%) patients, whereas 5 (1.6%) cases were found with pure non-TCC at the final pathology [Figure 1].

One case had SmCC in the proximal ureter and another case was proved to be adenocarcinoma in pelvicalyceal system in a 77-year-old male, who died after 5 months. Three patients had SCC of the renal pelvis (RP), and two of them were treated with radical nephrectomy of renal masses [Figures 2 and 3]. The clinical, histopathological characteristics and outcomes are listed in Table 1. The cancer-specific survival for non-TCC cohort is markedly decreased (log-rank = 0.01) compared to TCC patients. None of them had intravesical recurrence.

DISCUSSION

Non-TCC is a rare tumor of the upper urinary tract. In our series, the incidence is 1.6% – that is close to what is reported by Busby *et al.* among 474 UTUC patients (1.9%).^[4] However, Holmäng *et al.* reported 8% incidence for SCC only, 6%

were with pure SCC in their series.^[3] Similarly, Li and Cheung reported 8% SCC among 144 patients.^[2]

We may contribute the wide range of the incidence of non-TCC in the literature to the subjective pathologic reporting with pure or mixed non-TCC histological types. We have 33 patients (11%) in our series with squamous and glandular differentiation reported with TCC; that is also similar to the incidence in a large multi-institutional study (14%) that enrolled more than 1600 patients.^[9] Reporting these cases as pure SCC or adenocarcinoma may cause the difference in the incidence of non-TCC.

SmCC of the upper urinary tract is a neuroendocrine cell tumor. Positive staining for chromogranin AI, synaptophysin, and neuron-specific enolase confirm the diagnosis. Histopathologically, it is similar to their pulmonary counterpart with small, uniform cells with nuclear molding, scant cytoplasm, and nuclei containing finely dispersed chromatin [Figure 4].

The case in our series was in the ureter, and that is in accordance to many published series. Ouzzane *et al.* reported two cases of SmCC; both were in the ureter.

Adenocarcinoma of the upper urinary tract is a rare tumor, comprising less than 0.5% of the UTUC.^[4] It must be a pure adenocarcinoma with histopathological features of well-defined glands lined by typical cells with large nuclei and moderate amount of mucinous cytoplasm staining for carcinoembryonic antigen and mucin [Figure 5].

Based on the published case reports, the cancer survival varies for patients with adenocarcinoma of the upper tract. Two cases, one in the RP and the other in the ureter died 5 and 125 months, respectively, after the treatment.^[4] In another



Figure 1: Coronal contrast-enhanced CT showing marked hydronephrotic right kidney with upper ureteric soft tissue mass... Likely urothelial tumor

Table 1: Clinical, histopathological characteristics and outcome

Pathologic type	Age	Side	Preoperative HN	Tumor location	Tumor size (cm)	Surgical management	Grade	Stage	Follow-up (months)	Recurrent bladder tumor	Status	Cause of death
Small cell carcinoma	70	Right	Marked	Proximal ureter	22×15×10	Open NU + BCE	-	T2N0M0	7	No	DOD	Local recurrence
Adenocarcinoma	77	Left	No	RP, calyces	Nonreported	Open NU + BCE	Grade I	T1NxM0	5	No	DOD	Distant metastasis
7 SCC	46	Left	No	RP	15×12×9	Radical nephrectomy	Grade I	T3N0M0	10	No	DOD	Local recurrence
SCC	61	Left	No	RP	17×16×12	Open NU+BCE	Grade II	T1N0M0	14	No	AWNR	-
SCC	63	Left	Moderate	RP	15×7×7	Radical nephrectomy	Grade I	T3N1M0	5	No	DOD	Local recurrence

HN: Hydronephrosis, NU + BCE: Nephroureterectomy with bladder cuff excision, RP: Renal pelvis, SCC: Squamous cell carcinoma, DOD: Died of disease, AWNR: Alive with no recurrence

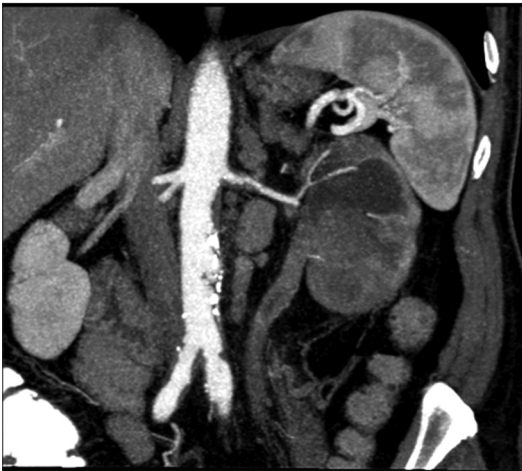


Figure 2: Coronal contrast-enhanced CT showing enhancing soft tissue mass inside left renal pelvis, lower calyx, left ureter and invading the parenchyma of lower pole. Likely left urothelial tumor with parenchymal invasion; multiple enlarged left peri, para-aortic and aortocaval lymph nodes



Figure 3: Axial contrast-enhanced computed tomography showing enlarged left kidney; the renal pelvis and calyces are the seat of large soft tissue lesion measuring (21 cm × 13.5 cm × 12 cm) with multiple renal stones. Findings can cope with left urothelial hypovascular mass. The right kidney showing multiple calyceal stones and parapelvic cyst (2 cm × 2 cm)

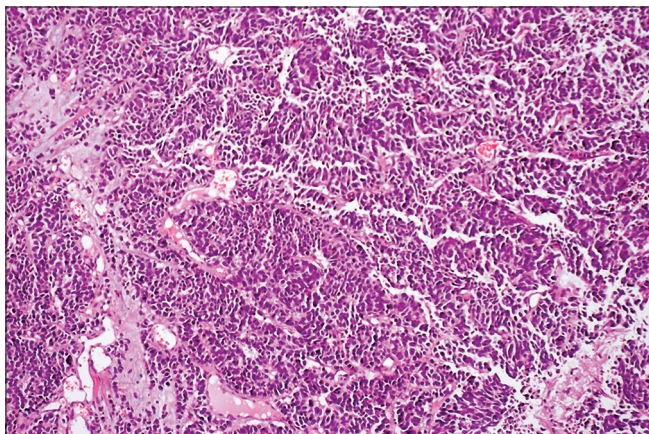


Figure 4: Small cell carcinoma of the ureter

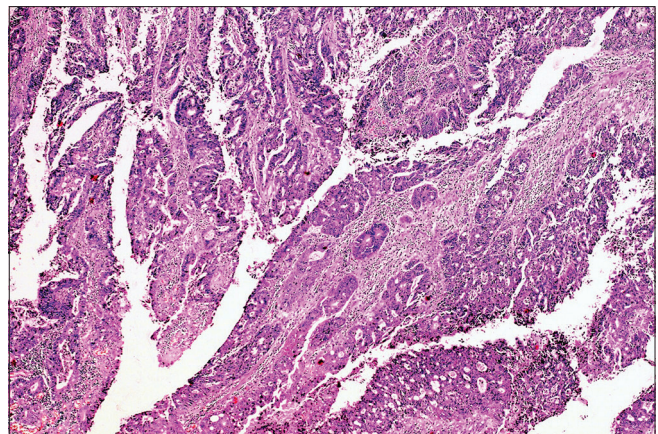


Figure 5: Grade 1 adenocarcinoma of the renal pelvis

case report, with two cases of T3 and T4 adenocarcinoma of clear cell type, one case died at 2 months, and the other patient missed the follow-up. Our case died 5 months after the surgery.

SCC is the most common among non-TCC type as it comprises 1–6% on non-TCC.^[3,5] Many risk factors may have a role in the pathogenesis of SCC: Chronic irritation,

long-standing urinary obstruction, and renal stones.^[2] Previous surgeries for renal stones, analgesic use, and radiotherapy were also considered as risk factors.^[3] One of our patients had hydronephrosis and the other had multiple stones [Figure 3]. SCC may be associated with paraneoplastic syndrome;^[10] however, the laboratory workup of our patients did not show any abnormal results.

SCC may mimic renal parenchymal tumors in its radiologic criteria; two out of three patients in our series were operated by radical nephrectomy for renal parenchymal tumors.

Histopathologically, SCC is characterized by sheets of cells with well-defined cell borders, deeply eosinophilic cytoplasm, and features of keratin pearls [Figure 6].

The three patients in our series had tumors in the RP and calyces; one also involved the upper part of the ipsilateral ureter. Similarly, 70% of SCC cases and among 808 patients with UTUC were in the RP!^[3]

Studies from UB carcinomas reflected the role of chronic irritation/infection in the pathogenesis of non-TCC. When the schistosomiasis was endemic in Egypt, the incidence of SCC and adenocarcinoma was reported to be 59% and 22%, respectively.^[11] Non-TCC incidence is much different than what was reported from a systematic review from Europe and North America that reported the incidence of SCC, SmCC, and adenocarcinoma of 3–5%, 0.5–2%, and <0.5%, respectively.^[6] Patients having such risk factors are advised to be counseled for possible development of non-TCC.

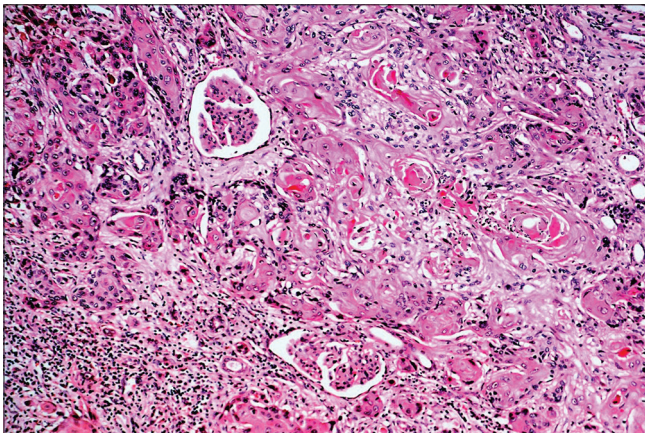


Figure 6: Grade 1 squamous cell carcinoma of the renal pelvis

Surgery is still the treatment of choice for non-TCC, whereas radiotherapy and chemotherapy have little benefit.^[2] Adjuvant chemotherapy was used in 11 patients; however, the median survival was only 5 months.^[12]

CONCLUSION

In our series, non-TCC of the upper urinary tract is rare (1.6%). It may exist with no known risk factors has a poor prognosis when compared to TCC, and it is seldom to have intravesical recurrences. New neoadjuvant and adjuvant therapies are hoped to improve the survival in such patients.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. *CA Cancer J Clin* 2007;57:43-66.
- Li MK, Cheung WL. Squamous cell carcinoma of the renal pelvis. *J Urol* 1987;138:269-71.
- Holmäng S, Lele SM, Johansson SL. Squamous cell carcinoma of the renal pelvis and ureter: Incidence, symptoms, treatment and outcome. *J Urol* 2007;178:51-6.
- Busby JE, Brown GA, Tamboli P, Kamat AM, Dinney CP, Grossman HB, et al. Upper urinary tract tumors with nontransitional histology: A single-center experience. *Urology* 2006;67:518-23.
- Assad Isa Kroon W, Robles García JE, Aguera Fernández LG, de Castro Barbosa F, Sánchez de la Muela PL, Rosell Costa D, et al. Pure squamous carcinoma of the ureter. Review of a case. *Arch Esp Urol* 1992;45:472-3.
- Dahm P, Gschwend JE. Malignant non-urothelial neoplasms of the urinary bladder: A review. *Eur Urol* 2003;44:672-81.
- Manunta A, Vincendeau S, Kiriakou G, Lobel B, Guillé F. Non-transitional cell bladder carcinomas. *BJU Int* 2005;95:497-502.
- Ploeg M, Aben KK, Hulsbergen-van de Kaa CA, Schoenberg MP, Witjes JA, Kiemeneij LA. Clinical epidemiology of nonurothelial bladder cancer: Analysis of the Netherlands Cancer Registry. *J Urol* 2010;183:915-20.
- Rink M, Robinson BD, Green DA, Cha EK, Hansen J, Comploj E, et al. Impact of histological variants on clinical outcomes of patients with upper urinary tract urothelial carcinoma. *J Urol* 2012;188:398-404.
- Diaz González R, Barrientos A, Larrodera L, Ruilope LM, Leiva O, Borobia V. Squamous cell carcinoma of the renal pelvis associated with hypercalcemia and the presence of parathyroid hormone-like substances in the tumor. *J Urol* 1985;133:1029-30.
- Ghoneim MA, el-Mekresh MM, el-Baz MA, el-Attar IA, Ashamalla A. Radical cystectomy for carcinoma of the bladder: Critical evaluation of the results in 1,026 cases. *J Urol* 1997;158:393-9.
- Blacher EJ, Johnson DE, Abdul-Karim FW, Ayala AG. Squamous cell carcinoma of renal pelvis. *Urology* 1985;25:124-6.