



ORIGINAL ARTICLE

Diagnosis of upper tract urothelial carcinoma—a comparative study of urinary cytology and surgical biopsy

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KEYWORDS

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Introduction Upper tract urothelial carcinoma (UTUC) is defined as urothelial carcinoma (UC) arising in the renal pelvis and ureter. Upper tract (UT) cytology and biopsy evaluation can be technically challenging. The aim of the study is to evaluate the diagnostic modality and sensitivity of urine cytology and ureteroscopic biopsy for the diagnosis of UTUC.

Material and methods All patients with UTUC who underwent radical nephroureterectomy or ureterectomy with preoperative cytology and/or biopsy from January 1, 2000 to September 30, 2011 at our institution were included in this study. The sensitivity of each diagnostic modality was calculated with respect to tumor grade, stage, and size.

Results A total of 143 cytology specimens and 54 biopsies from 65 patients were evaluated. For low-grade UTUC, the sensitivities for biopsy, lower tract cytology, and UT cytology were 68.4%, 27.3%, and 37.5%, respectively. These numbers were 82.9%, 40.7%, and 80.6% for high-grade UTUC. By combining the UT cytology and biopsy, the diagnostic sensitivities were increased to 87.5% for low-grade UTUC and 100% for high-grade UTUC. The consistency of tumor grade between biopsy and surgical specimen were 63.2% for low-grade UTUC and 68.6% for high-grade UTUC.

Conclusions Both UT cytology and biopsy showed higher sensitivity in detecting high-grade UTUC versus low-grade UTUC. The sensitivities of UT cytology and ureteroscopic biopsy in detecting high-grade UTUC were comparable. The sensitivity was greatly improved when these diagnostic modalities were combined. As expected, the selective UT cytology evaluation had superior sensitivity in detecting UTUC than did the lower tract cytology sampling.

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Introduction

Accurate preoperative diagnosis of upper tract urothelial carcinoma (UTUC) is essential for formulating an appropriate therapeutic strategy. Although imaging has a very important contribution,^{1,2} urinary tract cytology and biopsy diagnosis still play a crucial role in UTUC management.^{3,4} However, adequate ureteroscopic biopsies are difficult to obtain and may lead to diagnostic difficulties as shown by Tavora et al.⁴ who concluded that “the pathologists should recognize that in almost one of the four renal pelvic/ureteral biopsies, a definitive diagnosis cannot be made because of the inadequate tissue.” As a consequence of technical difficulties in obtaining adequate biopsies of the upper urinary tract,⁴ cytology plays an essential role in the diagnosis of UTUC. The sensitivity of urinary cytology in detecting urothelial carcinomas (UC) of all sites has been well-studied and ranges between 55% and 90%.⁵⁻⁸ Only a few upper tract (UT) cytology (ie, selective ureteral/renal pelvis cytology) studies on UTUC have been reported, with similar, albeit lower sensitivities, ranging between 43% and 78%.^{3,9-11}

The aim of this study was to better understand the diagnostic value of urinary cytology and ureteroscopic biopsy in detecting UTUC. To achieve this goal, we performed a retrospective cohort study of patients with UTUC managed at our institution, and we determined the sensitivities of urinary cytology and ureteroscopic biopsy in detecting UTUC, as well as the impact of tumor grade, size, and stage on the sensitivities of these diagnostic methods.

Material and methods

We performed a search of the electronic medical records to identify patients who were diagnosed with UTUC and subsequently underwent a radical nephroureterectomy or ureterectomy at our institution between January 1, 2000 and September 30, 2011. Patients who had no urinary cytology or ureteroscopic biopsy performed within a 6-month interval prior to surgery were excluded from the study. Patients with previously or concomitantly diagnosed UC of the bladder were excluded in order to allow for comparison for UT cytology with bladder barbotage specimens.

The tumors were staged according to the 2002 American Joint Committee on Cancer TNM (tumor, node, metastasis) classification,¹² and graded according to the 2004 World Health Organization/1998 International Society of Urologic Pathology consensus classification.¹³⁻¹⁵ At our institution, UT cytology cases are categorized in a 4-tier system: positive for UC (positive for high grade UC [HGUC]); suspicious for UC (suspicious for HGUC); atypical urothelial cells present (AUC); and negative (negative for malignancy). On the rare occasion when a true fibrovascular core is visualized and there is minimal cytologic atypia, a diagnosis of low-grade UC (LGUC) is rendered. The diagnosis “suspicious for HGUC” is only rendered when there are rare

cells (<10 cells) with the cytomorphologic features of HGUC; this category is analogous to the recently proposed AUC-H (atypical urothelial cells, cannot exclude high-grade urothelial carcinoma).² At most institutions, including ours, the urological management of these “suspicious” cases is the same as that of the “positive for HGUC” cases. As such, for the purposes of this study, these groups were combined when calculating the sensitivity of urinary cytology. Due to the uncertainty of the exact meaning and management of an “atypical” (AUC) diagnosis, analysis was done both considering AUC diagnoses as “positive” and as “negative” for sensitivity calculations. The urinary cytology evaluation was further subgrouped into upper tract (selective ureteral/renal pelvis washing or brushing) and lower tract ([LT], ie, voided urine and bladder barbotage) cytology.

Two-tailed *P* values were calculated by the Fischer exact test, based on 2 × 2 contingency tables. A *P* value < 0.05 was set for statistical significance. As the patient pool consisted of patients with confirmed UTUC alone, only sensitivity data could be calculated.

Results

We identified 80 patients who underwent radical nephroureterectomy or ureterectomy for UTUC from January 2000 to September 2011. Fifteen patients were excluded because they either did not have any cytologic specimens (*n* = 10) or did not have “adequate” preoperative urinary cytology or biopsies, including 2 biopsy specimens in which the “tissue” was lost during processing and 3 cytology cases in which the specimens were completely acellular and therefore “unsatisfactory” for cytologic evaluation. The study group consisted of 65 patients, 36 men ages 37 to 83 years (mean 68) and 29 women ages 51 to 89 years (mean 72), who had preoperative cytology (143 cytologic specimens from 59 patients), and ureteroscopic biopsies (54 biopsies from 53 patients). Of those 65 patients, 46 underwent testing by both modalities.

From the 54 preoperative biopsy specimens, 35 were from the renal pelvis and 19 from the ureters. Of the 143 urine cytology specimens, 59 were from the renal pelvis, 35 from the ureters, and 49 were bladder barbotage or voided urine specimens (Table 1).

The preoperative cytology results showed 79 cases that were positive or suspicious for UC (Fig. 1 depicts an example of HGUC), of which 5 cases (all renal pelvic brushing specimens) were reported as LGUC. An additional 25 cases were reported as AUC, and 39 cases were reported as negative for malignancy.

In none of the cases was LT cytology positive or suspicious for UC when UT cytology was negative. UT cytology had a significantly higher sensitivity than LT cytology did, independent of the assignment of AUC cases to the positive or negative categories (62 of 94 [66.0%] versus 17 of 49 [34.7%], *P* = 0.0004 if AUC was considered negative and

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