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Original contribution

# Urothelial carcinoma involving the ureteral orifice: a clinicopathologic analysis of 93 cases☆

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**Summary** Although tumors involving the bladder and ureter have been well described, there are only few studies in the pathology literature specifically analyzing tumors involving the ureteral orifice (UO). A search was performed for biopsy and resection specimens (transurethral resection, radical cystectomy/cystoprostatectomy, nephroureterectomy and bladder cuff resection) of urothelial carcinoma (UCa) involving the UO. Ninety-three cases were identified. Sixty-two (67%) patients were male. Mean patient age was 71 years (range, 43-91 years). Forty-two of 93 (45%) cases were invasive UCa (41 high-grade UCa; 1 low-grade UCa); 17/42 (40%) were invasive into muscularis propria. Tumor laterality was as follows: right side, 43 (46% of cases); left side, 41 (44%); bilateral, 4 (4.5%); and in 5 cases (5.5%), the laterality was not specified by the urologist. Seven cases of UCa with variant histology were also identified. Five patients had lymph node (LN) metastasis at the time of resection, and another 3 presented with LN or distant metastasis after resection (range, 4-38 months). Although this study focused primarily on the index tumor involving the UO (Group 1 cases are those with only UO involvement), in 70/93 (75%) cases (Group 2 cases), at least one other tumor was located at another site within the bladder. The fact that the majority of cases (75%) had tumors located at other sites of the bladder, emphasizes that careful examination of the UO needs to be performed by both urologists and pathologists when examining cases of UCa of the bladder.


## 1. Introduction

Urothelial carcinoma (UCa) is the ninth most common malignancy worldwide and has a higher incidence in the Western world [1]. UCa is more common in men than women with a ratio of 3:1 and has a high rate of recurrence (up to 80%) [2,3]. Studies of UCa of the bladder have identified smoking as the most important risk factor, in the Western world. Urinary bladder tumors are random in their distribution within the bladder [4]. Although tumors of the urinary bladder and ureter have been well described, there is very limited pathological data specifically analyzing tumors involving the ureteral orifice. Jancke et al studied the risk of recurrence based on the location of the tumor near the ureteral orifice and showed that the primary tumor adjacent to the ureteral orifice is associated with recurrence but not progression [5]. Chou et al showed that superficial UCa near the ureteral orifice is predictive of higher risk of recurrence of tumor in the upper urinary

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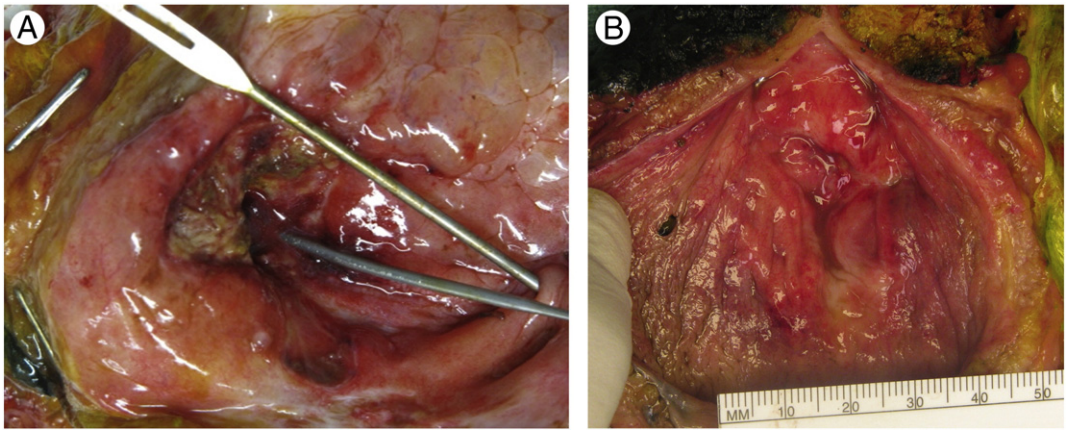


**Fig. 1** A and B, Gross photographs of UCa involving the ureteral orifice.

tract [6]. In this study, we sought to identify cases of UCa from our institution in which the index tumor involved the ureteral orifice, and characterized the clinical and pathologic features of these tumors.

## 2. Materials and methods

A search was made through our Urologic Pathology files and Expert Consultation files of the senior author for biopsy and resection specimens, including transurethral resection (TUR), radical cystectomy (RC), radical cystoprostatectomy (RCP), and nephroureterectomy and bladder cuff resection (NUBC) cases of UCa involving the ureteral orifice at our institution. Patient demographics, tumor grade, size, laterality, variant histology and depth of invasion were documented. When available, follow-up data were also obtained. The cases were also stratified into 2 groups (Group 1: Cases with tumors confined to the ureteral orifice only, and Group 2: Cases with tumor involving the ureteral orifice and an additional concurrent site).

For the purpose of this study, recurrence was defined as reappearance of the tumor either at the primary site of resection (local recurrence) or at a different site (distant metastasis or lymph node metastasis) following primary resection.

This study was completed following the guidelines of and with approval from our institutional review board.

## 3. Results

### 3.1. Demographics and gross examination features

Ninety-three patients had tumor involving the ureteral orifice (either unifocal or multifocal) and were included in this study. The mean age was 71 years (range, 43-91 years), and incidence in men was twice that of the women. Of these 93 cases, 23 patients had tumor involving only the ureteral orifice, and 70 patients had multifocal tumors that also involved another site within the bladder or beyond. Thirty-eight of these patients underwent radical resection including 7 patients with NUBC and 31 cases of RC/RCP. There was no difference in terms of laterality of the location of the tumor (right: 43, left: 41, bilateral: 4, not specified: 5), but the majority of the tumors were unilateral (84 unilateral versus 4 bilateral tumors, 5 not specified). The tumors ranged in size from microscopic to 8.0 cm (Fig. 1A and B).

### 3.2. Microscopic examination features

Microscopic evaluation of the tumors involving the ureteral orifice revealed predominantly non-invasive urothelial tumors (51/93 cases, 55%) of which 17 were low-grade UCa (Fig. 2A), 22 were high-grade UCa (Fig. 2B), and 12 UCa in situ (Fig. 2C). Forty-two of the 93 cases had an invasive high-grade UCa (Fig. 3A). Seven of the invasive high-grade UCa cases had divergent differentiation and include 2 cases with micropapillary variant, 2 cases with sarcomatoid differentiation, 2 cases with squamous differentiation and 1 case with nested/microcystic features (Fig. 3B-E).

### 3.3. Surgical margin status and tumor staging of radical resection specimens

With regards to the surgical margin status, 5 cases had positive margins for either UCa in situ or invasive UCa. Interestingly, only one of these 5 cases had a recurrence of the disease at a later time point (see local recurrence section for further details). Of the 31 patients that underwent RC/RCP, 39% of cases (12/31) were staged pT1 or below with 4 cases of pTis, 1 case of pTa, 4 cases of pT1, and 3 cases of pTx; 22% of cases (7/31) were staged pT2, 26% of cases (8/31) were staged pT3 and 13% of cases (4/31) were staged pT4. Seven patients that underwent nephroureterectomy, 29% of cases (2/7) were pTa, another 29% of cases (2/7) were pT1, and the remaining 42% of cases (3/7) were staged as pT3. Five of the 38 patients that underwent resection had lymph node metastasis at the time of resection (2 cases of pN1 and 3 cases of pN2).