CORRELATION BETWEEN FILLING DEFECT PATTERNS ON UROGRAPHY AND PATHOLOGIC STAGING OF URETERAL TRANSITIONAL CELL CARCINOMAS

Yi-Lun Lee, Shu-Pin Huang, Min-Chen Shih, Yii-Her Chou, and Chun-Hsiung Huang
Department of Urology, Chi-Shan Hospital, and Departments of Urology and Radiology, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan.

Although a filling defect within the ureter is the most common finding with ureteral transitional cell carcinomas (TCCs), little is known about the correlation between filling defect patterns and pathologic findings. This study was conducted to address this. Between January 1995 and January 2003, 126 pathologically confirmed TCCs of the ureter were included in our study. We classified urographic filling defects into four patterns: ovoid, polypoid, infiltrating, and plaque-like. The correlation between different filling defect patterns and pathologic findings was assessed using Pearson’s Chi-squared and logistic regression methods. There were 28 (22%) ovoid filling defects, 42 (33%) polypoid filling defects, 37 (29%) infiltrating filling defects, and 19 (15%) plaque-like filling defects. Infiltrating and plaque-like filling defects were significantly associated with more advanced disease compared to ovoid and polypoid filling defects (odds ratio, 6.75; 95% confidence interval, 3.04–14.98; \( p < 0.0001 \)). Our results suggest that filling defect presentations may signify different invasive behavior among TCCs. The distribution of ovoid, polypoid, infiltrating, and plaque-like filling defect patterns is significantly different between superficial and advanced ureteral TCCs. We suggest that classifying the filling defect patterns of ureteral TCCs may provide important preoperative information for planning treatment and predicting outcome.

Key Words: neoplasm, transitional cell carcinoma, ureter, urography (Kaohsiung J Med Sci 2003;19:447–52)

Transitional cell carcinoma (TCC) of the ureter is not common worldwide, representing only 1% of all genitourinary malignancies [1–3]. However, ureteral carcinoma is relatively common in Taiwan [4–7]. Urographic examinations, including intravenous pyelography (IVP), retrograde pyelography (RP), and antegrade pyelography (AP), are important tools in detecting the tumor and defining its extent and location [1,3,8]. The most common radiographic finding in ureteral carcinoma is the presence of a filling defect within the ureter [9,10]. Although various filling defect patterns have been reported with ureteral TCCs [1,8,11], only a few studies have focused on the association between filling defect patterns and pathologic findings. Here, we report a large series of ureteral TCCs and analyze the correlation between filling defect patterns and pathologic staging.

MATERIALS AND METHODS

Between January 1995 and January 2003, patients at our institution with histopathologically confirmed TCC of the ureter and with complete radiographic and histologic data...
were eligible for inclusion in the study. Computed
tomography was obtained in all cases and all patients
underwent at least one urographic examination (IVP, RP, or
AP). RP or AP was usually performed when IVP failed to
localize the lesion or when patients had renal insufficiency.

Urographic films were reviewed by an independent
radiologist (MCS) who was blinded to clinical and pathologic
data. Filling defects on urography were divided into four
patterns by their shape: ovoid, polypoid, infiltrating, or
plaque-like [11]. We defined ovoid as a single, rounded,
nodular, exophytic lesion (Figure A); polypoid as a papillary,
lobulated, exophytic lesion (Figure B); infiltrating as an
extensive, straggling, sessile, broad-based lesion (Figure
C); and plaque-like as a thickened-wall constriction with
overhanging edges and strand-like contrast filling
appearance (Figure D). Surface regularity, goblet sign,
stipple sign, concomitant calcification, and pseudo-
diverticulum were also recorded. We used the most clearly
defined images from IVP, RP, and AP to categorize the
patterns of the filling defects.

Pathologic staging was based on the classifications
proposed by Batata et al [12]: stage A is defined as
submucosal infiltration, stage B as muscular invasion, stage
C as periureteral involvement, and stage D as extension to
adjoining structures, regional lymph node metastases, or
distant spread. Stage A was considered superficial disease
because it was limited to the submucosal layer. Stages B, C,
and D were considered advanced disease because invasion
reached at least the muscle.

Pearson’s Chi-squared and logistic regression methods
were used to examine the association between various
filling defect patterns and pathologic staging. Data are
presented as odds ratio (OR) and 95% confidence interval
(95% CI). A p value of less than 0.05 was considered
statistically significant. Data analysis was performed using
SPSS version 8.01 (SPSS Inc., Chicago, IL, USA).

**RESULTS**

Of 134 histopathologically confirmed cases of TCC of the
ureter between January 1995 and January 2003, eight cases
were excluded due to incomplete radiographic and
histologic data. A total of 126 cases were enrolled in the
study. Mean age at diagnosis was 66.5 years (range, 26–85).
There were more male (54%) than female patients (Table 1).
Most tumors were located in the upper third of the ureter;
the left ureter was more frequently involved than the right
ureter. There were similar numbers of superficial and
advanced tumors (Table 1). Gross hematuria was the most
common symptom, occurring in 70% of patients. Flank
pain, urinary frequency, dysuria, lower abdominal pain,
and fever were less common symptoms. Seven patients
(6%) were asymptomatic and were diagnosed incidentally
on ultrasonography after presentation with hydronephrosis.

Filling defect patterns were determined by RP (80 cases,
63%), AP (39 cases, 31%), and IVP (7 cases, 6%). Polypoid
filling defects were most common (33.3%), followed by
infiltrating (29.4%), ovoid (22.2%) and plaque-like (15.1%)
filling defects (Table 2). Most lesions (81.7%) manifested
with an irregular surface. The goblet sign was found in
30.2% of lesions and the stipple sign in 19.8%. Seven lesions
(5.6%) showed concomitant calcification. There was no
pseudodiverticulum.

The distribution of ovoid, polypoid, infiltrating, and
plaque-like filling defects was significantly different between
superficial disease and advanced disease (Chi-squared test,
Different filling defect patterns in ureteral carcinoma

DISCUSSION

Ureteral carcinomas are mostly located in the lower third of the ureter [12–14]. In northern Taiwan, interestingly, Yang et al documented an unusually high incidence of upper urinary tract urothelial carcinoma and suggested that geographic factors or genetic predisposition might contribute to this phenomenon [4]. Our data show that the upper third of the ureter is most frequently involved in ureteral TCCs in southern Taiwan. The possible cause of this finding in southern Taiwan is undetermined. Various authors consider that the high incidence of upper urinary tract carcinomas in southern Taiwan is due to the fact that it is an area that is endemic for blackfoot disease [5–7]. Evidence suggests that the arsenic content and fluorescent substances in artesian well water are a possible etiology in blackfoot-endemic areas [15–19], but further investigation is needed to determine whether this is so. There was no significant difference in filling defect presentations among the various locations of ureteral carcinomas in our study.

IVP, RP, and AP are inexpensive and are examinations which can be easily performed to detect ureteral tumors and define their extent and location [1,3,8]. IVP is the primary initial examination for ureteral lesions, but only 6% of the tumors in our study could be clearly seen with their filling defect on IVP films. RP and AP films usually provide more satisfactory delineation of the filling defect and the precise filling defect pattern. RP and AP are more reliable than IVP and clearly revealed approximately 94% of filling defects in our study.

Both the goblet sign and stipple sign are specific features of TCC of the ureter [20,21]. However, in our study, only 30.2% of cases had the goblet sign and only 19.8% had the stipple sign. Wasserman et al reported that ureteral pseudodiverticula were frequently associated with uroepithelial malignancy [22], but we observed no

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<tr>
<th>Table 2. Radiographic presentation of filling defects in 126 ureteral transitional cell carcinomas</th>
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<td><strong>n (%)</strong></td>
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<tr>
<td>Shape</td>
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<tr>
<td>Ovoid</td>
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<td>Polypoid</td>
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<td>Plaque-like</td>
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<td>Regular</td>
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<td>Irregular</td>
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<td>Goblet sign</td>
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<td>Stipple sign</td>
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<td>Concomitant calcification</td>
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<td>Pseudodiverticulum</td>
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<th>Table 3. Comparison of filling defect patterns with tumor stage</th>
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<tr>
<td><strong>Tumor stage</strong></td>
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<td><strong>Filling defect pattern</strong></td>
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<td></td>
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<tr>
<td>Ovoid</td>
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<tr>
<td>Polypoid</td>
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<tr>
<td>Infiltrating</td>
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<td>Plaque-like</td>
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Chi-squared test, \( p < 0.0001 \).
pseudodiverticulum in our study. The role of these specific signs may need to be further elucidated.

The distribution of the four filling defect patterns was statistically different between superficial and advanced ureteral TCCs ($p < 0.0001$) (Table 3). Infiltrating and plaque-like filling defects were significantly associated with advanced TCCs, while ovoid and polypoid filling defects were associated with superficial TCCs (OR, 6.75; 95% CI, 3.04–14.98; $p < 0.0001$) (Table 4). These findings are compatible with the view that grossly polypoid and pedunculated urothelial tumors are less invasive than sessile or flat lesions [1]. Our results demonstrated that ureteral TCCs have different invasive behavior and can be identified through various filling defect patterns seen on urographic films.

Total nephroureterectomy with excision of the bladder cuff is the standard therapy for ureteral malignancy [2,13,14]. However, some authors advocate nephron sparing surgery (NSS), including segmental ureteral resection or transureteral endoscopic management in selected patients [23–26]. These methods are controversial due to observed recurrence rates of 12% to 50% [23–28]. To our knowledge, no study has made recommendations on how to preoperatively select patients for NSS for ureteral carcinomas. Based on our urographic and pathologic findings, we postulate that an aggressive treatment strategy is needed for infiltrating and plaque-like filling defects due to the possibility of invasive tumor behavior, whereas NSS may be appropriate for less invasive ureteral TCCs with ovoid and polypoid filling defects.

Our study has some limitations due to its retrospective design. We attempted to reduce observer bias by blinding one independent radiologist to the clinical and pathologic data; the influence of observer bias should be minimal. A large-scale, prospective clinical trial is warranted to further validate our findings.

In conclusion, infiltrating and plaque-like filling defect patterns are significantly associated with advanced TCCs of the ureter, while ovoid and polypoid filling defect patterns are associated with superficial TCCs of the ureter. The filling defect pattern on urography may provide important preoperative information to aid treatment planning and deserves further investigation to validate its application in clinical management.

**REFERENCES**


**Table 4. Correlation between filling defect patterns and tumor stage in ureteral transitional cell carcinomas**

<table>
<thead>
<tr>
<th>Filling defect pattern</th>
<th>Superficial disease</th>
<th>Advanced disease</th>
<th>OR (95% CI)</th>
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<tr>
<td></td>
<td>$n$ (%))</td>
<td>$n$ (%)</td>
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<tr>
<td>Ovoid or polypoid</td>
<td>47 (67)</td>
<td>23 (33)</td>
<td>1.00</td>
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<tr>
<td>Infiltrating or plaque-like</td>
<td>13 (23)</td>
<td>43 (77)</td>
<td>6.75 (3.04–14.98)</td>
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OR = odds ratio; CI = confidence interval. Logistic regression test, $p < 0.0001$. 
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