

Bilateral High-Grade Invasive Papillary Urothelial Carcinoma of the Renal Pelvises Following Radical Cystoprostatectomy

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Introduction

Uroepithelium is a special type of epithelium that lines the proximal urethra, bladder, ureter, renal pelvis and calyceal system.¹ Cancer of the uroepithelium, known as urothelial carcinoma, can occur in any structure containing uroepithelium, with 5-10% of the cases occurring in the upper urinary tract (UTUC) and the remaining cases occurring in the lower urinary tract (LTUC).^{2,3} Cancer in the upper urinary tract is generally silent and is twice as common in the renal pelvis than the ureter.^{2,3} Urothelial carcinoma has a male predisposition (2:1) and is normally diagnosed between the ages of 70 and 90 years of age,² with a median age of 73 for men^{3,4} and 69 for women.⁴ When UTUC is diagnosed, the gold standard for treatment is a radical nephrectomy.⁵ Urothelial carcinoma can be divided into two types: flat and papillary.^{6,7} The tumor can then be further classified as non-invasive (in-situ) vs. invasive and low grade vs. high grade.⁶ Additionally, there are many histological variants of urothelial carcinoma, especially in the renal pelvis.⁷ A few examples of the histological variants include the plasmacytoid, microcytic, and nested variant.⁸ The varied histological morphologies present a diagnostic challenge and affect prognosis and clinical management of the patient.

Patient Case

This is an 80 year-old man, whom, over the course of more than a decade, transitioned from high grade non-invasive papillary urothelial bladder carcinoma to high-grade bilateral invasive papillary urothelial carcinoma of the renal pelvises. The first time bladder cancer was diagnosed, TURBT was performed and von Brunn's nests were detected histologically. Over the next six years, bladder urothelial carcinoma occurred three more times. On the third recurrence, a radical cystoprostatectomy with ileal conduit was performed. Seven years later, the patient presented with bilateral urothelial carcinoma of the renal pelvises and right ureter, which was staged pT3Nx and pTa, respectively. Both kidneys were removed via laparoscopic bilateral radical nephrectomy with surgical excision of the ileal conduit. During the procedure, while freeing the right kidney, a hardened area on the anterosuperior-medial perinephric fat was noted, representing either extravascular extension or lymphadenopathy. The left kidney (specimen A) and the right kidney, ureter, and ileal conduit (specimen B) were extracted and sent down to the laboratory after being freed from all posterior, superior (sparing of adrenal gland) and lateral attachments. A third specimen consisted of the stoma and small portion of the skin. Follow up information on the patient is unavailable.

Materials and Methods

Cassettes submitted by the Pathologists' Assistant for both right and left kidney included:

- Bowel margin
- Vascular Margin
- Tumor with ureter at uretero-pelvic junction
- Tumor with renal vessel
- Tumor to renal sinus fat
- Tumor to renal parenchyma
- Tumor to hilum/peri-renal sinus fat margin
- Section of possible tumor in the vessels near calyx
- Uninvolved Gerota's fascia/peritoneum
- Uninvolved section of bowel mucosa
- Additional sections of the ureter
- Possible additional viable sections of tumor
- Tumor to renal parenchyma
- Tumor invasion into peri-renal fat

When grossing cases of urothelial carcinoma, extensive sampling of not only the tumor, but the entire specimen, is crucial. Ample sampling of the specimen helps ensure correct histopathological diagnosis, despite the numerous challenges caused by the histological variants of urothelial carcinoma and the varied pelvicalyceal anatomy.

Results

Macroscopic pathological findings:

The left radical nephrectomy specimen (left kidney, ureter, perinephric fat and minute fragment of bowel) weighed 910 gm and measured 22.0 (S-I) x 14.0 (M-L) x 9.0 (A-P) cm. Bi-valving revealed a unifocal, necrotic, friable tumor measuring 10.5 (S-I) x 8.5 (M-L) x 4.5 (A-P) cm extending 1.0 cm into the ureter and involving the uretero-pelvic junction, renal sinus fat, renal calyces, parenchyma and possible invasion into the perirenal fat (**Figure 1**). The remaining parenchyma was compressed and had no definite cortico-medullary junction.

The right radical nephrectomy specimen (right kidney ureter, perinephric fat and ileal conduit) weighed 980 gm and measured 20.0 (S-I) x 15.0 (M-L) x 8.0 (A-P) cm. The ureter measured 4.0 cm. Bi-valving revealed a unifocal, friable, necrotic tumor measuring 7.0 (S-I) x 6.5 (M-L) x 3.0 (A-P) cm invading into the uretero-pelvic junction, renal sinus fat, renal calyces, and parenchyma (**Figure 2**). The cut surface of the specimen revealed a yellow-red to brown, semi-lunar area (7.2 S-I x 1.7 -L, x 3.5 A-P cm) within the renal parenchyma on the opposite side of the hilum (**Figure 2**). One lymph node candidate (1.0 x 1.0 x 2.0 cm) was identified near the hilum.

Microscopic Pathological findings:

Microscopic evaluation of the hematoxylin and eosin slides (H&E) of the right and left kidney demonstrated urothelial carcinoma of the renal pelvis with invasion into the peri-pelvic fat (**Figure 3**) and renal parenchyma. For both the right and left kidney specimen, additional pathological findings in the non-neoplastic renal parenchyma included glomerulosclerosis, tubulointerstitial disease, atherosclerosis, and chronic inflammation.



Figure 1: Gross image of the bi-valved left radical nephrectomy specimen, demonstrating the unifocal, friable lesion with invasion into adjacent structures.

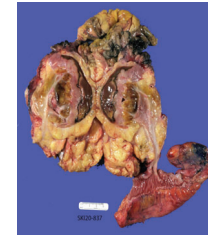


Figure 2: Gross photograph of the right radical nephrectomy specimen, with ileal conduit, demonstrating the unifocal, friable lesion with invasion into adjacent structures. An additional lesion opposite of the hilum demonstrates possible hematoma, necrosis, or separate tumor.

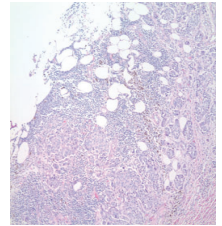


Figure 3: Microscopic image of a section of the left renal pelvis with malignant cell invasion into renal pelvic adipose tissue.

Discussion

Diagnosis

The gross and microscopic findings were consistent with bilateral high-grade invasive papillary urothelial carcinoma of the renal pelvises. An additional finding included high-grade non-invasive papillary urothelial carcinoma of the right ureter.

Staging

Based on the AJCC staging guidelines, the bilateral kidney tumors were both staged as pT3, since there was invasion into the peri-pelvic fat and into the renal parenchyma.⁹ With both kidneys, the regional lymph nodes could not be assessed. As a result, the cancer was given the stage pNX.⁹ The urothelial carcinoma of the right ureter was staged separately and was assigned as pTa (per AJCC guidelines), since the papillary urothelial carcinoma was non-invasive.⁹

Diagnostic challenges of Urothelial Carcinoma

A specific diagnostic challenge that presented in this case was the appearance of von Brunn's nest in the first presentation of bladder carcinoma. Von Brunn's nests, a benign entity, can easily be mis-recognized as the nested variant and vice versa.^{7,8,10} Macroscopically, this variant is hard to identify.¹⁰ Therefore, it is essential that the tumor is adequately sampled. Although in this particular case the von Brunn's nests were detected in the bladder carcinoma, extensive sampling should still take place when working with tumors in the upper urinary tract, as von Brunn's nest are more commonly found in the renal pelvis and the ureter.⁷

Another challenge in the diagnosis of urothelial carcinoma that presented in this case is the fact that the histology within the pelvicalyceal system is tremendously varied.¹¹ In the minor calyces, there is a fluctuating amount of muscularis propria.¹¹ Not only does this make muscularis propria invasion harder to diagnose, but it also makes invasion into surrounding renal parenchyma and perirenal/peripelvic adipose tissue more challenging to microscopically detect.¹¹ As adipose tissue is admixed normally within the lamina propria, muscularis propria and surrounding soft tissues,¹¹ a patchy muscularis propria adds on an additional level of diagnostic complexity. Another challenge when dealing with tumors of the renal pelvis system is extension of the tumor into the distal collection system. This extension can easily be diagnosed and staged as invading the renal parenchyma, when truly the invasion is limited to the ductal system.¹¹ As clinical management for Tis/Ta UC is radically different than T3 staged carcinoma, accurate diagnosis is essential. As a result, it is important for pathologists' assistants to extensively sample and submit sections to include the following: tumor to adjacent renal and ureter parenchyma, tumor to peripelvic and perirenal adipose tissue, and unremarkable parenchyma with margins.

Acknowledgements

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