High-grade T1 Bladder Cancer at the Ureterovesical Junction

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Challenging Case
A 56-year-old healthy man with a negative medical history presented with a single episode of gross hematuria. A CT urogram disclosed normal kidneys and an entirely normal left upper urinary tract. On the right, however, there was a dilated ureter to the right ureterovesical junction. A ureterocele appeared to be present at this location, though there appeared to be a solid component within the ureterocele. The rest of the work-up was normal, including all laboratory tests and chest radiographs. A cystoscopic examination and transurethral resection (TUR) of the right hemitrigone was performed. The bladder was entirely normal except for the raised area over the right orifice. When the area was resected a papillary-appearing tumor was evident under the surface. The orifice became apparent and was dilated. A ureteroscopy was not performed. A cold cup biopsy of the distal ureter was obtained in order to preserve the integrity of the ureterovesical junction. The appearance of the ureter was perfectly normal until just above the ureterovesical junction on the CT urogram (Fig. 1). The pathology revealed high-grade T1 urothelial carcinoma of the bladder with uninvolved muscle present in the specimen from the trigone and papillary high-grade Ta from the small ureteral biopsy.

Further diagnostic work-up that may help with the evaluation would include a ureteroscopy of the involved ureter. This would provide needed information regarding the extent of the disease within the more proximal ureter. Although a CT urogram can identify most solid upper tract lesions, direct vision via ureteroscopy should provide a more accurate assessment of the status of the urothelium. If a suspected region of carcinoma in situ of the ureter was visualized, ureteroscopic biopsy or brushing could be performed to assess for multifocality. A restaging TUR of the bladder trigone would be necessary to determine the appropriateness of a bladder-sparing approach. A complete resection of all invasive disease and the confirmation of no involved muscle would be a prerequisite for consideration of intravesical therapy for the T1 component.

If we assume that the ureter has high-grade disease only in the distal ureter, the recommended treatment should be surgical excision. In the setting of a very distal lesion with no evidence of proximal involvement, a distal ureterectomy and reimplantation would be a reasonable approach, keeping in mind that the remaining portion of that upper tract is at risk for recurrence in the future.

The bladder lesion is of concern as well. A thorough evaluation of the extent of invasion helps in determining the risk of progression. Multiple studies have demonstrated the importance of the depth and extent of invasion of the lamina propria. For small volume, superficial lamina propria invasion confirmed on restaging TUR of the bladder tumor (TURBT), intravesical therapy with Bacillis Calmette-Guerin (BCG) would be an appropriate initial treatment. In contrast, a T1 lesion that demonstrates extensive and deep involvement of the lamina propria would be best managed in a similar fashion to muscle-invasive disease. Many times the information on the restaging TURBT, taken together with the result of the initial resection, provides important information that alters therapy.

If more extensive involvement of the lamina propria is noted, the patient should be counseled on the role of early radical cystectomy. This discussion should center on the evaluation of risks, and the patient should be informed that with the substantial risk of progression from an initial high-volume T1 lesion, early cystectomy should provide the highest cure rate. The lower ureteral lesion would be resected at the time of cystectomy, making sure to check a frozen section of the margin before comple-
tion of the urinary diversion. This young patient with early-stage disease would be an appropriate candidate for a nerve-sparing cystoprostatectomy and orthotopic reconstruction. If he has normal preoperative erectile function, he would be expected to have an excellent functional outcome with respect to both voiding and potency.

**Expert Commentary: Dr. Dinney**

The initial steps in the management of this challenging case identified several critical patient-care issues that need to be addressed before proceeding to definitive treatment, namely the determination of the clinical stage of the bladder tumor at the ureteral orifice, the ability to control this lesion, and the limits of the ureteral involvement. The first step in addressing these issues is to repeat cystoscopy and re-resection of the tumor bed to identify the presence of residual tumor. Even in the face of a seemingly complete resection, the incidence of persistent tumor within the resection site is reported to be as high as 65%. Upon re-resection of a T1 lesion in which muscularis propria is present in the specimen, the incidence of documented muscularis propria involvement approaches 15%. Furthermore, even if persistent T1 disease is documented, cystectomy should be strongly considered because the risk of progression following intravesical therapy is prohibitive.

It could also be argued that if persistent invasive cancer is not documented upon re-resection, cystectomy is still indicated because of the inherent difficulties in accurately staging invasive lesions at the ureteral orifice. The presence of hydronephrosis further adds to the dilemma because its presence strongly suggests the presence of occult muscle-invasive bladder cancer. The fact that the orifice itself is dilated may indicate that the hydronephrosis is truly related to the presence of a ureteroceles, but the findings are not definitive, and this alternate explanation does not alleviate concern.

Restaging is also indicated to delineate the extent of the tumor within the ureteral orifice and direct appropriate management. Unfortunately, there are no dependable landmarks that can direct the depth of resection of a lesion in this location other than the transition from deep muscle to perivesical fat. If no gross evidence of papillary tumor is apparent within the intramural ureter following repeat resection, a final deep margin should be obtained. Because the patient may balk at cystectomy, random bladder biopsies (including biopsies of the prostatic urethra) are indicated if a wide local excision of the ureteral orifice with nephroureterectomy or resection of the distal ureter is contemplated. If these additional biopsies are positive, it would strengthen the argument for cystectomy. Finally, ureteroscopy should be contemplated either at the time of the re-resection or later as a staged procedure to ensure that the remainder of the upper urinary tract is free from malignancy.

Final recommendations depend upon the results of these subsequent procedures. The doctor should begin the discussion with the patient by emphasizing that radical cystectomy offers the best opportunity for control of a cT1 bladder tumor at the ureteral orifice, especially one associated with hydronephrosis. The decision to proceed with cystectomy is clear if the re-resection identifies persistent T1 or T2 neoplasia. If the patient resists, the doctor should discuss bladder preservation as an option if the re-resection identifies noninvasive cancer or carcinoma in situ but with the caveat that adequate staging of a lesion at the ureteral orifice is limited, and a decision to preserve the bladder in the face of occult invasive disease could have fatal consequences.

Management of the ureteral tumor is also directed by information garnered at restaging. If tumor is identified in the proximal ureter or renal pelvis, nephroureterectomy should be offered. If tumor persists only within the distal ureter, a distal ureterectomy could be performed either in conjunction with radical cystectomy (preferred) or with a wide resection of the bladder at the ureteral orifice, assuming that the random bladder biopsies and prostate biopsies are negative. If this course of action was favored by the informed patient, the doctor should first offer a course of intravesical therapy. Finally, if the re-resection of the bladder was negative and the ureteral tumor appeared to be adequately controlled transurethrally and if cystectomy was resisted, the doctor should offer a course of intravesical BCG, with careful re-staging with repeat TUR and ureteroscopy following treatment.