A Case of Synchronous Bilateral Upper Urinary System Urothelial Carcinoma

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Abstract
Synchronous bilateral upper urinary tract urothelial cancer (UTUC) is a very rare form of urothelial cancer. In patients with high-risk unilateral UTUC, radical nephroureterectomy (RNU) is the gold standard treatment. However, there is no consensus on the treatment for synchronous bilateral UTUC. Evaluation of the patient and the tumor is recommended. Bilateral nephron-sparing surgery (NSS) was performed on a 53-year-old patient who presented with high-risk synchronous bilateral UTUC, and the outcome was reported.

Keywords
Synchronous; Bilateral Upper Urinary Tract; Urothelial Cancer; Treatment

Özet

Anahtar Kelimeler
Senkronize; Bilateral Üst Üriner Sistem; Ürotelyal Kanser; Tedavi
## Introduction

Upper urinary tract urothelial carcinomas (UTUC), which constitute 5–10% of urothelial tumors, are mostly unilateral and less than 5% are synchronous bilateral urothelial tumors [1]. The incidence of UTUC peaks in those 70–90 years old [2]. Although UTUC is less frequent than bladder cancer, at the time of diagnosis 60% of tumors have invasive characteristics. Despite the lack of prospective studies of UTUC, patients with UTUC can be subdivided into low- and high-risk groups, and their treatments planned accordingly. Nephron-sparing surgery (NSS) can be performed in low-risk patients who meet the following criteria: unifocal tumors smaller than 1 cm in diameter with a low grade based on cytology and histopathology of an ureterorenoscopy (URS) biopsy specimen and no evidence of invasion based on multidetector-row computed tomography (MDCT). High-risk UTUC patients have one of the following: hydronephrosis, multifocal disease, history of cystectomy performed for bladder cancer, or high-grade tumors based on cytology or histopathological examination of the URS biopsy specimen. For tumors larger than 1 cm, a radical nephroureterectomy (RNU) is recommended [3]. Concomitant cases with synchronous bladder and UTUC have been reported, while cases with synchronous high-risk bilateral UTUC are rare [4]. Our patient underwent NSS. Here, we report the preoperative, intraoperative, and postoperative imaging results.

## Case Report

A 53-year-old male farmer presented with intermittent left flank pain and hematuria for 2 months. The patient had a 20 pack-year history of smoking, but no additional systemic disease. His family history was unremarkable. Urinary ultrasound revealed a 1.5-cm mass in the right renal pelvis and grade 3 pelvicalyceal ectasia of the left kidney. MDCT showed that the right kidney was smaller in size, a 15-mm contrast-enhancing tumor was observed in the right renal pelvis, as well as grade 1 pelvicalyceal ectasia. The left kidney had increased in size and had grade 3 pelvicalyceal ectasia. A mass nearly 2 cm in diameter was detected in the distal end of the left ureter. On MDCT, no evidence of extrapelvic or extrareteral invasion or intra-abdominal lymphadenopathy was detected (Figures 1 A, B). A chest X-ray showed no metastases. The serum creatinine was 2.8 mg/dL. With a presumptive diagnosis of UTUC, the patient underwent a cystoscopy and bilateral rigid URS. Cystoscopy did not reveal any tumors inside the bladder lumen. Punch biopsies were obtained from the fragile tumor mass localized in the distal end of the left ureter and from a papillary tumor in the anteromedial aspect of the right renal pelvis. In the same session, nephrostomy tubes were inserted bilaterally following URS. At follow-up, the serum creatinine was 1.2 mg/dL, and average daily urine output from the right and left nephrostomy tubes was 1000 and 1500 mL, respectively. A histopathological analysis of the biopsy material excised from the left ureter was reported as papillary-type transitional cell carcinoma histological grade 1 with invasion of the lamina propria. The histopathological analysis of the right renal pelvis indicated papillary-type transitional cell carcinoma histological grade 2 with invasion of the lamina propria. As such, 2 weeks after the first operation, the existing nephrostomy tract was dilated up to 28Fr to access the right renal pelvis with the patient in the prone position, and then a 24Fr resectoscope was inserted through the access tract to perform percutaneous tumor resection, and coagulation of the tumor base using a Ho:YAG laser at the end of the resection (Figure 2 A, B). Then, the patient was turned into the supine position, the distal ureter was excised together with the bladder cuff, and an extravesical ureteroneocystostomy was performed (Figure 2 C). The patient was discharged on postoperative day 5 with implanted nephrostomy tubes without any complications. The histopathology was similar to that of the first biopsy specimen. As the patient was in the high-risk group, he received instillations of six weekly doses of Bacillus Calmette-Guérin (BCG) solution diluted to 50 mL (IMMUCYST, Sanofi-Aventis, France) delivered through the right and left nephrostomy tubes in equal portions starting 3 weeks after the operation. During all of these procedures, no apparent complications were observed. After the BCG therapy was finished, the nephrostomy tubes were removed. Two months later, the patient underwent a diagnostic cystoscopy and bilateral URS. No tumor recurrence was observed at the surgical sites or in the bladder. No atypical cells were detected in a cytology sample. The patient was followed at 3-month intervals for the first 2 years, then at 6-month intervals for a total of 30 months. At every follow-up visit, biochemical, radiological (abdominal ultrasound or MDCT, chest x-ray), cystoscopy, and flexible URS examinations were performed, and samples were obtained for cytological analysis. No radiological, endoscopic, or pathological recurrence was observed over 30 months of follow-up.

## Discussion

Urinary tract urothelial cancer can develop during the treatment of superficial bladder tumors or it can occur de novo. In 17% of the cases, concomitant bladder tumors are present [5]. Synchronous bilateral UTUC is rare and has been reported in 0.8–4.7% of the cases [4,6,7]. Guidelines recommend follow-up and a treatment algorithm for unilateral UTUC; data is available for synchronous bilateral UTUC in only a few retrospective case series. Many demographic and tumor-related factors play a role in planning treatment for patients with synchronous bi-
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The main treatment alternatives are bilateral or unilateral RNU and contralateral or bilateral NSS. These treatment alternatives can be realized using open, laparoscopic, or endoscopic methods [4,6,7]. Fang et al. [6] compared the oncological outcomes of 39 synchronous bilateral and 853 unilateral UTUC patients. The median age of the patients with bilateral tumors was 68 years. They observed that bilateral tumors differed significantly from unilateral tumors in terms of female predominance, presence of preoperative renal failure, previous or concomitant bladder tumor, low-grade tumors, papillary structure, and smaller tumor size. In cases with reduced renal function or larger tumors, a bilateral RNU was preferred, while in most (67.6%) of the cases unilateral RNU plus unilateral NSS was preferred. The disease recurred in 36.8% of the cases, while bladder tumors recurred in 31.6%. The oncological outcomes resemble those of unilateral UTUC, and the median cancer-specific survival rate was 81.2% [6].

In 15 cases of synchronous bilateral tumors published by Holmang and Johansson [8], the use of phenacetin-containing analgesics was an etiological factor in 20% of the cases. Unilateral resection was feasible in eight patients, while a bilateral nephrectomy was performed in three patients. The eleven cases that underwent surgery had a mean survival time of 84 months [8].

Our 53-year-old patient was somewhat young for developing UTUC. As risk factors, he was a smoker with no history of bladder carcinoma or phenacetin use. The smaller size of his right kidney could not be explained. Despite its smaller size, the mean parenchymal thickness of this functional kidney was 1.3 mm and the mean daily urine output was 1 L. Histopathological examination of the URS biopsy specimen was reported as high-risk bilateral UTUC. The guidelines recommend RNU for high-risk unilateral UTUC, while there are no recommendations for synchronous bilateral UTUC. Considering the patient’s young age, absence of signs and symptoms of renal failure, absence of metastasis, apparent resectability of both tumors, and the patient’s preference, we decided to perform bilateral NSS. To decrease the recurrence rate in such a high-risk patient, BCG solution was instilled through both nephrostomy tubes postoperatively. During 30 months of follow-up, no evidence of recurrence has been detected radiologically, endoscopically, or histopathologically.

In conclusion, synchronous bilateral UTUC is very rare, and there is no treatment algorithm. The role of NSS in the treatment of UTUC has increased. Before deciding on RNU, which has an irreversible treatment outcome, we think that NSS should be performed in compliant patients with localized disease. Prospective studies with larger patient populations should examine this issue.

Competing interests

The authors declare that they have no competing interests.

References