CASE REPORT
Urooncology

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Urothelial Carcinoma of the Upper Urinary Tract That Becomes Resectable After Neoadjuvant Chemotherapy: A Case Report and Review of the Literature

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Abstract

Upper tract urothelial carcinoma (UTUC) is less common than bladder cancer, but its incidence is increasing. Neoadjuvant chemotherapy (NAC) has been the treatment focus for locally invasive and high-grade UTUC. Herein, we aimed to present a case of a locally advanced non-metastatic UTUC, which was thought to be unresectable due to local invasion, but surgically treated successfully after NAC. A 64-year-old male patient was admitted to another hospital because of right flank pain, which was not accompanied by macroscopic haematuria. He did not have comorbidities in his anamnesis, but he had a history of smoking 40 packs/year. A locally invasive right kidney tumour was detected in cross-sectional imaging performed at another hospital. He underwent surgery in that hospital, but radical nephroureterectomy could not be performed because of local invasion. He presented to our urology department. He was subsequently started with cisplatin-based NAC, which led to the resolution of local invasion. After NAC, right radical nephroureterectomy and ipsilateral bladder cuff excision with subcostal and Gibson incisions were performed. No signs of mass invasion or lymph node involvement were detected intraoperatively. He was examined 3 months after surgery. On cystourethroscopy, the bladder was normal and cytology was benign. No recurrence or metastasis was detected on the whole-body computed tomography. NAC is one of the valuable multimodal treatment options, enables surgery in locally invasive UTUC and contributes positively to survival rate.
Keywords: Oncology, urooncology, urothelial carcinoma, nephrectomy, nephroureterectomy, neoadjuvant chemotherapy

Introduction

Upper tract urothelial carcinoma (UTUC) accounts for 5% of urothelial cancers. Although UTUC is less common than bladder cancer, its incidence is increasing recently (1,2). Radical nephroureterectomy (RNU) and excision of the ipsilateral bladder cuff is the standard surgical procedure for the treatment of UTUC, and surgical treatment can often be curative alone (3). In recent years, organ-sparing approaches have also been considered in some selected cases. Although the standard treatment is RNU, recurrence rates after the surgical approach in locally advanced diseases are quite high, and growing evidence shows the role of both adjuvant chemotherapy (AC) and neoadjuvant chemotherapy (NAC) (4,5). Especially in locally advanced disease, the pathological downstaging (PD) rates by NAC have been shown to contribute positively to survival (6).

Herein, we will present a case of a locally advanced non-metastatic UTUC, which was thought to be unresectable due to local invasion but successfully surgically treated after NAC.

Case Presentation

A 64-year-old male patient was admitted to another hospital because of right flank pain, which was not accompanied by macroscopic haematuria. He did not have comorbidities in his anamnesis, but he had a history of smoking 40 packs/year.

Computed tomography urography was performed after ultrasonography and detected a mass in the right kidney. A 60×85×100 mm^3 infiltrative mass extending to the renal pelvis was detected in the upper and middle calices of the kidney (Figure 1). At the level of the renal hilus, two lymph nodes of 25 mm and 26 mm in diameter were observed anterior to the inferior vena cava. The mass infiltrated the perirenal fat. No metastatic focus or extra pathology was detected in chest computed tomography.

On cystourethroscopy, no tumour was observed in the bladder, so RNU was arranged in the first hospital, but RNU could not be performed. His operation report stated that the abdominal wall muscles were cut through the right subcostal incision and

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entered into the abdominal cavity. The right colon was released, and the right kidney was reached. The surgery was terminated because renal pedicle release was not possible due to inferior invasion of the vena cava.

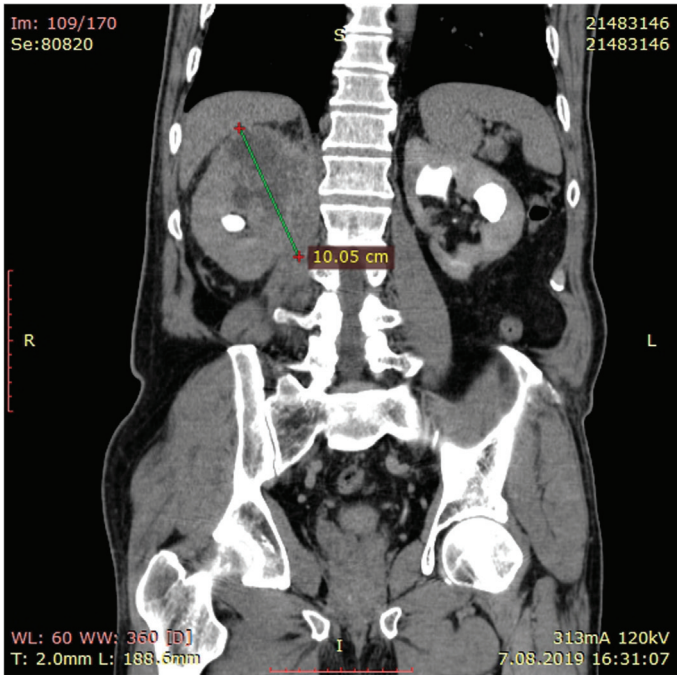

Figure 1. Before neoadjuvant chemotherapy

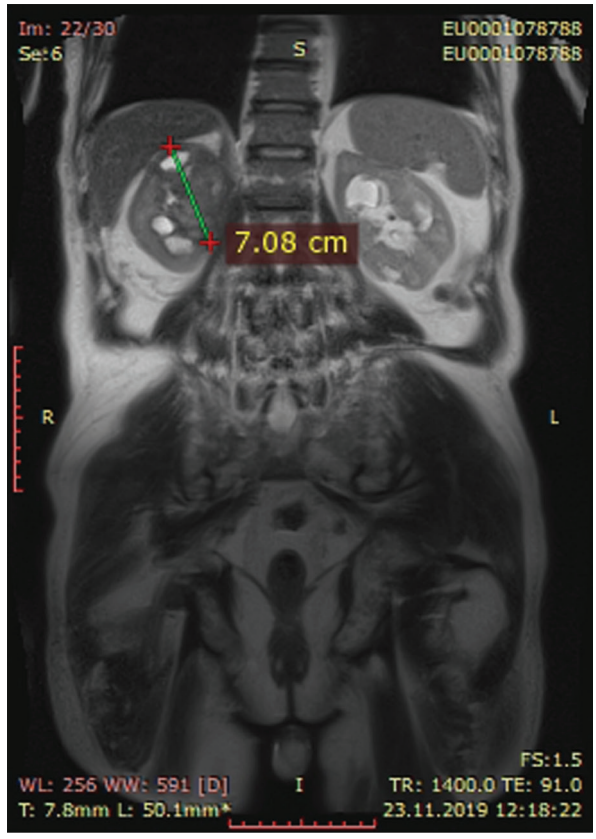

Figure 2. After neoadjuvant chemotherapy

He was referred to our urology department, and a renal biopsy was then performed. NAC was initiated because his renal biopsy histopathological examination finding was compatible with urothelial carcinoma and a local invasive mass was found in the right kidney. The patient received two cycles of gemcitabine (1,000 mg/m^2) and cisplatin (80 mg/m^2). Magnetic resonance imaging was performed for restaging after NAC, which revealed that the mass in the right kidney regressed to 53×60×70 mm^3, and the two pre-existing lymph nodes disappeared (Figure 2).

Right RNU and ipsilateral bladder cuff excision with subcostal and Gibson incisions was performed. No signs of mass invasion or lymph node involvement were detected intraoperatively (Figure 3). Histopathological diagnosis was interpreted as pT4 urothelial carcinoma, and the surgical margins were clear (Figure 4).

The patient was examined 3 months after surgery. On cystourethroscopy, the bladder was normal and cytology was benign. No recurrence or metastasis was detected on the whole-body computed tomography. Written informed consent was obtained from the patient.

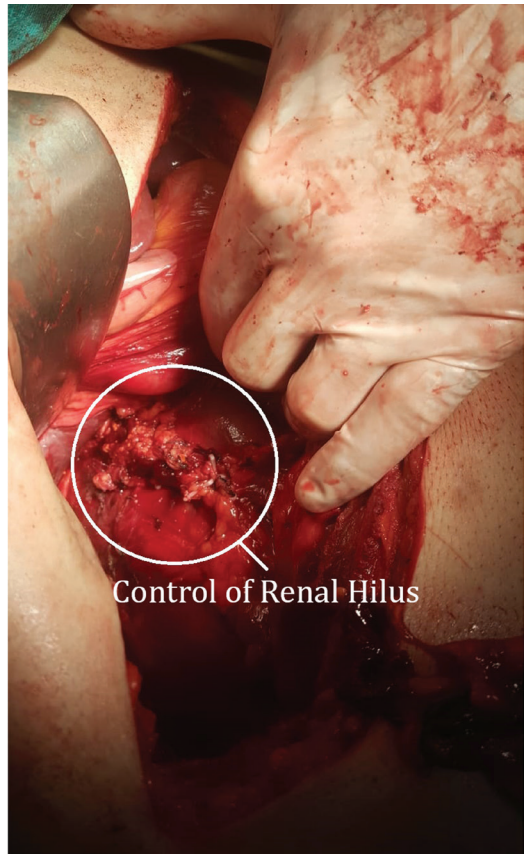

Figure 3. Renal hilus control

Discussion

Evidence on the effectiveness of NAC is based on the results of AC treatment for bladder cancer (1). Compared with AC, NAC may be

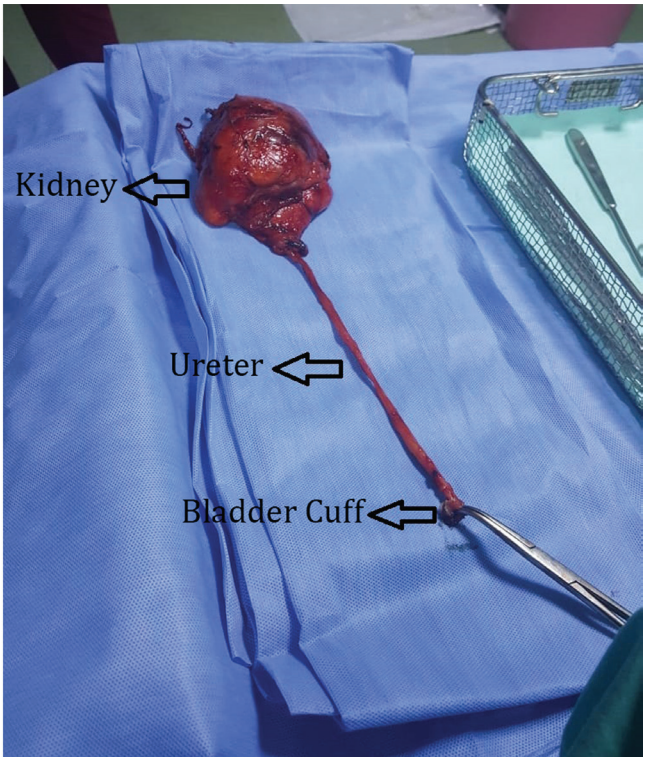

Figure 4. Postoperative view of specimen

considered as a more effective treatment option for UTUC, because some patients cannot receive cisplatin-based AC due to postoperative kidney function impairment (7-9). Cisplatin-based NAC can result in higher pathological complete response (PCR) and PD rates than other chemotherapy regimens, but creatinine clearance must be >50 mL/min for the suitability of this treatment (10). Therefore, preoperative chemotherapy treatment may be more advantageous.

Although UTUC is morphologically similar to bladder cancer, different phenotypically and genotypically malignancies exist because of the high rate of locally advanced disease development (11). The 5-year overall survival (OS) rates of locally invasive UTUC stage T2 and T3 were 73% and 40%, respectively. The median survival time was 6 months in T4 stage (12). Although RNU is the standard treatment for high-grade and locally advanced UTUC, its recurrence rate is quite high. Thus, NAC as treatment for bladder cancer might be considered to treat occult micrometastasis and provide PDs (8). In a recent meta-analysis, OS, cancer-specific survival and progression-free survival in patients receiving NAC were 57%, 59% and 45%, respectively, and PDs increased by 4.76-fold in the NAC-treated group (13). Compared with PCR after NAC, the PD is a stronger prognostic factor for survival rates (6,14). In a prospective study investigating the pathological response to NAC, the PCR rate was 14% and the PD was 60% (10). In our case, the pathological lymph nodes disappeared in magnetic resonance imaging performed after NAC.

As stated in the European Association of Urology guideline, the NAC regimen used in bladder cancer is also effective in the treatment of UTUC (15). However, some patients may lose their chance to undergo surgery, or surgical treatment may be delayed due to the toxicity of chemotherapy after NAC (16). In a study of 61 patients who received NAC for high-grade UTUC, only one patient developed sepsis, but he eventually recovered, and none of the patients had lost their chances for surgery and they have progressive disease (17).

NAC cycle is still controversial for UTUC. A delay of >90 days for radical cystectomy was reported to be associated with a poor prognosis (18). In studies investigating NAC for UTUC, the tumour response was evaluated after two cycles of NAC within 90 days, in line with the recommendations for invasive bladder cancer treatment, and surgery was planned (19,20). Patients with insufficient tumour response (stable or progressive disease) received three or four cycles of NAC (20). Currently, only a few prospective randomised trials are underway for UTUC (21,22). These studies will shed light on NAC for UTUC. In our case, re-imaging was performed to evaluate tumour response after two cycles of NAC. After obtaining a tumour response, we decided to perform surgery.

Despite these data, NAC, which has level 1 evidence in locally advanced BC, has not been the standard treatment in locally advanced and high-grade UTUC, owing to the lack of prospective randomised studies (23).

Upon presentation to our department, we considered that the patient was an RNU candidate, but the case was judged as unresectable due to local invasion. As a result, we decided to initiate NAC. Thereafter, local invasion was resolved, and surgery was feasible and successfully performed. NAC is one of the valuable multimodal treatment options that should be kept in mind because it facilitates surgery in locally invasive UTUC and contributes positively to survival rate.

Ethics

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.D., F.K., S.K., A.Ş., Concept: M.D., Design: M.D., Data Collection or Processing: M.D., Analysis or Interpretation: F.K., S.K., A.Ş., Literature Search: M.D., Writing: M.D.

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