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Successful Kidney-Sparing Systemic Therapy for a High-Risk Ureteral Carcinoma Case

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Abstract
Upper tract urothelial carcinoma (UTUC) refers to the malignancies located from renal calices toward the end of the ureter and could be classified as renal pelvis carcinoma and ureteral carcinoma. For high-risk UTUC cases with a normal contralateral kidney, radical nephroureterectomy is the standard treatment. As for low-risk UTUC cases or solitary kidney cases, kidney-sparing therapy may be a better choice. Besides, to prevent postoperative recurrence, systemic therapy should be applied, though the investigation is still ongoing. In this case report, we reported a rare case diagnosed with high-risk ureteral carcinoma, but he underwent kidney-sparing therapy due to chronic kidney disease. Recurrence has occurred after segmental ureterectomy. But through the utilization of ablation, bladder instillation, and tislelizumab, endoscopy and CT were normal in the follow-up (the patient refused to take washings from the upper urinary tract) for more than a year. In all, the utilization of ureteroscopic retrograde tumor ablation, BCG bladder instillation, and tislelizumab injection to treat high-risk ureteral carcinoma for kidney-sparing therapy have filled in the gap in this field, which should be promoted to help more patients in similar situations.

Introduction

Upper tract urothelial carcinoma (UTUC) refers to the malignancies located from renal calices toward the end of the ureter and could be classified as renal pelvis carcinoma and ureteral carcinoma, while around 20% of UTUC cases also suffer from concurrent bladder cancer [1]. The risk factors of UTUC include smoking, phenacetin, aristolochic acid, etc. [2]. Diagnostic ureteroscopy through flexible ureteroscopy could visualize the ureter, renal pelvis, and collecting system and take biopsy for suspicious neoplasm. The determination of tumor grade heavily relies on ureteroscopic biopsy, which assists in making decisions between radical nephroureterectomy (RNU) and kidney-sparing therapy with the help of imaging findings and urinary cytology [3]. For high-risk

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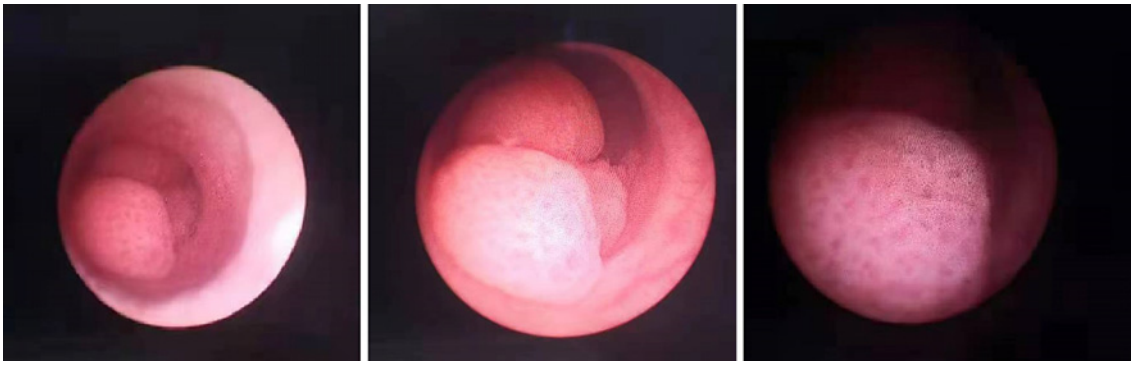

Fig. 1. Three cauliflower-like neoplasms were found in the left proximal ureter.

UTUC cases with a normal contralateral kidney, RNU is the standard treatment [4]. As for low-risk UTUC cases or solitary kidney cases, kidney-sparing therapy such as ureteroscopic retrograde tumor ablation, percutaneous antegrade tumor ablation, and segmental ureterectomy may be a better choice [5]. However, to prevent postoperative recurrence, systemic therapy should be applied, though the investigation is still ongoing [6].

In this case report, we reported a rare case diagnosed with high-risk ureteral carcinoma, but he underwent kidney-sparing therapy due to chronic kidney disease (CKD). Recurrence has occurred after segmental ureterectomy, but through the utilization of ablation, bladder instillation, and tislelizumab, endoscopy was normal in the follow-up for more than a year.

Case Report

A forty-four-year-old man has come to our hospital due to hematuria for 1 week, and ultrasound showed that there were multiple calculi in the left kidney. A few days later, ureteroscopy with holmium laser lithotripsy was performed. However, during the surgery, three cauliflower-like neoplasms were found in the left proximal ureter (shown in Fig. 1). Apart from lithotripsy, we have checked that there was no neoplasm in all left renal calices through flexible ureteroscope. Besides, biopsies of the neoplasms were also taken from the ureter, and later results have shown that they were high-grade papillary urothelial carcinomas. Moreover, after the surgery, renal emission computed tomography has suggested that the patient may also suffer from CKD, while the injury of the right kidney was more severe than that of the left one. Besides, we got to know that he has taken Aristolochia for medical use without the permission of doctors, which may result in ureteral carcinoma. Because of his renal function, the patient asked for kidney-sparing therapy regardless of high-risk pathological finding. Later, segmental ureterectomy of the left side was conducted, and pathological finding of the carcinoma was the same as the first time.

Three months later, urethrocystoscopy was performed for postoperative check, and a cauliflower-like neoplasm was found 1 cm away from the left ureteral orifice in the bladder (shown in Fig. 2). The renal pelvis was also checked, but there was no neoplasm in it. Biopsy was taken from the neoplasm in the bladder, and later pathological finding showed that it was urothelial carcinoma in situ. Five days later, transurethral resection of bladder tumor (TURBT) was conducted.

Another 3 months later, urethrocystoscopy was performed again. A cauliflower-like neoplasm was found in the right-top wall of the bladder, and three neoplasms were found in the calices. Four days later, TURBT and ureteroscopic retrograde tumor ablation were performed. Biopsies were also taken, and later they suggested that there were high-grade papillary urothelial carcinomas in the calices and chronic inflammation in the bladder. After the operation, tislelizumab (200 mg, ivgtt) and BCG (120 mg, bladder instillation) were applied regularly for target therapy and chemotherapy.

The postoperative follow-up via endoscopy and CT (the patient refused to take washings from the upper urinary tract) has been more than a year since the TURBT and ureteroscopic retrograde tumor ablation. Urethrocystoscopy has not detected neoplasm, and CT has not detected metastasis in the periodic review.

Discussion

The patient has suffered from ureteral carcinoma at a relatively young age, which possibly owing to taking Aristolochia without the permission of doctors. Aristolochia is a kind of Chinese herbal medicine that contains aristolochic acid and would cause UTUC and CKD, which has been listed as group 1 carcinogen [7]. Through renal emission computed tomography, we found that the patient also suffered from CKD, which was the reason that he asked for kidney-sparing therapy.

According to the data from other doctors, in around 25% of UTUC cases, the disease was multifocal [8]. The disease may relapse easily, especially in high-risk cases. Another study of 16 UTUC patients treated with kidney-sparing

Fig. 2. A cauliflower-like neoplasm was found 1 cm away from the left ureteral orifice in the bladder.

therapy showed that metastases occurred in 15 patients [8]. In all, it is of great significance for high-risk UTUC kidney-sparing cases to be treated with systemic therapy. A review summarized that chemotherapy through bladder instillation could have 11% risk reduction and immunotherapy could lengthen the disease-free time of the patients [8].

Through pathology finding, the patient was a high-risk UTUC case according to the guidelines from the European Association of Urology (EAU) [3]. For high-risk UTUC cases, RNU is usually used to achieve a relatively low recurrence rate. However, due to the renal dysfunction of this patient, kidney-sparing therapy should be taken into consideration, which could effectively protect renal function [9]. It was true that in this case, the carcinoma recurred after segmental ureterectomy, but the utilization of ablation, bladder instillation, and target therapy did effectively prevent the tumor from recurring in the follow-up for more than a year. And of course, the renal function of this patient has been well protected.

The use of tislelizumab should be highlighted in the systemic therapy. Tislelizumab is an anti-programmed death receptor 1 (PD-1) monoclonal IgG4 antibody and could inhibit the binding of PD-1 and programmed death ligand 1 (PD-L1) to suppress tumor growth, which has been applied to treating various tumors including UTUC. In fact, tislelizumab is not a commonly used PD-1 monoclonal IgG4 antibody in treating UTUC. But a case report has reported that tislelizumab could be a good choice for high-risk UTUC with kidney-sparing systemic therapy, which enlightened us a lot [10].

Statement of Ethics

This study protocol was reviewed and approved by the Ethical Committee of The First Affiliated Hospital of Zhengzhou University, approval number 2023-KY-0355. Written informed consent was obtained from patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

P.Y. and X.L. wrote the manuscript. Y.Y. contributed to the manuscript revision. P.X. and H.W. contributed to the conception of the study. All authors read and approved the submitted version.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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