De Novo Papillary Urothelial Carcinoma at a Previous Ureteroneocystostomy Site for Benign Ureteral Injury

Hongzoo Park
Department of Urology, Kangwon National University Hospital, Kangwon National University School of Medicine, Chuncheon, Korea

Ureteroneocystostomy is a good treatment option for iatrogenic ureteral injury. Common complications at ureteroneocystostomy sites are strictures, stone formation, urinary infections, fistulas, and ureteral leaks. Here, we report a rare occurrence of urothelial carcinoma occurring at the site of a previous ureteral reimplantation. A 57-year-old female presented in the Emergency Department with left flank pain and chills. She had undergone a left ureteroneocystostomy with Boari flap due to iatrogenic ureteral obstruction during a laparoscopic left ovarian cystic mass excision 2 years ago. Computed tomography revealed left ureteral obstruction by the tumor at the neo-ureterovesical junction site. Both anterograde and retrograde ureteral catheterization approaches failed. We conducted a left percutaneous nephrostomy and administered antibiotics. Urine cytology was negative. We performed a left ureterovesical obstructive mass excision and Yang-Monti ileal ureter reconstruction. Biopsy of the ureteral-obstructing tumor revealed a low-grade papillary urothelial carcinoma. The patient's symptoms and signs improved after surgery. To the best of our knowledge, this is the first report of a de novo urothelial carcinoma at the site of previous ureterovesical junction surgery. Urothelial carcinoma should be considered as one of the causes of stricture after ureteroneocystostomy. (Korean J Urol Oncol 2020;18:68-72)

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Corresponding Author: Hongzoo Park
Department of Urology, Kangwon National University Hospital, 156 Baengnyeong-ro, Chuncheon 24289, Korea
E-mail: amcmd@daum.net
Tel: +82-33-258-9478, Fax: +82-33-258-2455
ORCID: https://orcid.org/0000-0002-4953-5079

Most urothelial carcinomas occur in the bladder and about 5%–10% occur in the upper urinary tract. The risk factors for upper tract urothelial carcinomas (UTUCs) include environmental factors, such as Balkan endemic nephropathy; cigarette smoking; analgesics, such as phenacetin; and genetic factors, such as Lynch syndrome. The risk factors of urothelial bladder cancer (UBC) include cigarette smoking, infection with Schistosoma haematobium, analgesics, thiazolidinediones, occupational carcinogen exposure, and genetic factors. However, there have been no reports associating ureteroneocystostomy (UNC) procedures, such as Boari flap procedures, with the risk of UBC or UTUC. Moreover, the usual complications of ureteral reconstruction include strictures, obstructions, urolithiasis, hematuria, urinary tract infections, and fistulas, but cancer has not been reported to be a complication of UNC. To the best of our knowledge, this is the first report of de novo papillary urothelial carcinoma occurring at the site of a previous UNC.

CASE REPORT

This case review was conducted according to all guide-
lines outlined in the Declaration of Helsinki. Written informed consent for publication of this case report was obtained from the patient.

A 57-year-old female presented in the Emergency Department with left flank pain and chills lasting 2 days. Her vital signs were stable, except for a fever of 38.0°C. Two years ago, she underwent a laparoscopic left ovarian cystic mass excision due to a unilocular cystic mass in the left adnexa area (Fig. 1A). After obstetrical surgery, she experienced left flank pain that progressed gradually. A computed tomography (CT) image showed a low ureteral obstruction (Fig. 1B). We first conducted a left UNC procedure with Boari flap. After the procedure, her symptoms and signs improved. One week after surgery, her ureteral catheter was removed (Fig. 2A). Two months after surgery, the patient had no flank pain, fever, or azotemia. She received no further follow-up until she visited our Emergency Department due to left flank pain and chills. She was a non-smoking housewife with no family or medical history of cancer, diabetes mellitus, or hypertension. A routine hematologic examination showed leukocytosis (white blood cell, 12,000/µL). Her biochemical profiles were within normal limits, except for the presence of azotemia (serum creatinine, 1.8 mL/dL). Analysis of midstream urine showed many red blood cells /high-power field (HPF), many white blood cells /HPF, and a few epithelial cells. The urine culture showed no growth. Urine cytology was negative.

She was treated with antibiotics and painkillers. CT urography showed a tumor obstruction at the ureterovesical junction site of the previous surgery (Fig. 2B). There was no evidence of abnormal mucosal bladder lesions in the cystoscopic exam, except for an obstruction at the left ureteral orifice. We failed to find the left ureteral orifice to insert a ureteral catheter into the left ureter. Thus, we placed a
percutaneous nephrostomy tube into the left renal pelvis. However, we failed to place the antegrade ureteric catheter due to ureteral obstruction.

After her general condition improved, we performed a left ureterovesical obstructive mass excision and Yang-Monti ileal ureter reconstruction. A round, firm, 2-cm tumor was seen at the neo-ureterovesical junction site of the previous UNC procedure (Fig. 3). There were no nodal enlargements in the pelvic area. Histochemical examination of the specimen obtained by surgical resection revealed low-grade, non-invasive papillary urothelial carcinoma (Fig. 4). Tumor resection margin was negative.

Her symptoms and signs improved after the surgery and her serum creatinine level returned to normal (1.1 mL/dL). CT image showed no evidence of left urinary tract obstruction and the discrete glomerular filtration rate of the left kidney determined by a 99mTc-diethylenetriamine pentaacetic renal scan improved from 29.4 mL/min to 41.6 mL/min in three postoperative months (Fig. 5).

According to the standard treatment option of low-grade, low stage upper urinary tract carcinoma, we did not perform adjuvant chemotherapy or radiotherapy. She underwent a cystoscopic exam every three months and a CT scan every 6 months and had no recurrence for 2 years.

**DISCUSSION**

To our knowledge, this is the first case to document the occurrence of urothelial carcinoma at the site of ureteral re-implantation after a UNC procedure. The patient had no known risk factors for UTUC or UBC, such as cigarette smoking, infection with *Schistosoma haematobium*, occupa-
Fig. 5. Computed tomography (CT) and nuclear medicine image 3 months after the second ureteroneocystostomy. (A) CT image. (B) 99mTc-diethylentriamine pentaacetic renal scan image. GFR: glomerular filtration rate.

tional carcinogen exposure, history of drug use, or family history of cancer. It is possible that her urothelial carcinoma was caused by genetic factors. However, it is presumed that her previous UNC procedure, rather than genetic factors, was associated with the carcinoma since she had no family or past medical history of cancer and the urothelial carcinoma occurred at the exact reimplantation site.

Some de novo malignancies following surgery have been reported. Kimura et al. reported an increase in the overall incidence of de novo malignancies after heart transplantation. After solid organ transplantation, patients developed de novo bladder cancer. Antunes et al. reported that 61 de novo urologic malignancies have been recorded after renal transplantation. In these three reports, all de novo cancer patients were treated with posttransplantation immunosuppressants. Thus, the cases in these reports were likely caused by immunosuppressive therapy, rather than by surgery itself. The patient in our case had no previous history of immunosuppressive therapy.

The exact cause of urothelial carcinoma during the perioperative period of the first UNC procedure in this patient is unclear. However, several assumptions can be made. Cancers are now known to be caused by both irritation and infectious agents. There were many irritating factors in the cancer site of our patient. First, during the laparoscopic left ovarian cystic mass excision, the left lower ureter was damaged by cautery. Second, during the perioperative period of the first UNC procedure, the same site was damaged by stricture, a double J stent, and decreased blood supply due to dissection. There were also infective factors present in this patient. The obstruction that occurred after the laparoscopic left ovarian cystic mass excision caused a temporary urinary tract infection until the first UNC procedure. Asymptomatic cystitis might also have been present after first UNC procedure.

Common complications of UNC include strictures, obstructions, urolithiasis, hematuria, urinary tract infections, and fistulas. UNC with Boari flap is a bladder flap technique of the distal ureter. The complications of UNC with Boari flap may not be significantly different from those of other UNC techniques. Urothelial carcinoma should be considered as one of the causes of stricture after UNC.

In summary, we encountered a de novo papillary urothelial carcinoma that occurred at the site of a previous UNC. We resected the tumor by open surgery. The possibility of urothelial carcinoma should be considered during the follow-up of patients undergoing UNC procedures.

CONFLICT OF INTEREST

The authors claim no conflicts of interest.

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