

PRIMARY ADENOCARCINOMA OF THE URETER : REPORT OF A CASE

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The patient was a 66-year-old man who presented with asymptomatic hematuria. Left hydronephrosis was observed on drip infusion pyelography (DIP), and retrograde pyelography (RP) was performed because the image of the ureter was poor. On RP, stenosis was observed in the left ureter at the L5 vertebral level. The same findings were obtained by antegrade pyelography in combination with nephrostomy. A white-colored tumor was observed at the site of stenosis by flexible pyeloscopy, and biopsy was performed. Adenocarcinoma was identified by histopathological examination. Total left renal nephroureterectomy was performed after its diagnosis as primary adenocarcinoma of the ureter (T2, N0, M0). To our knowledge, this is the 12th case reported in Japan. (Hinyokika Kyo **53** : 645–648, 2007)

Key words : Adenocarcinoma, Ureter

INTRODUCTION

Adenocarcinoma of the renal pelvis and ureter is a very rare malignant tumor. Primary adenocarcinoma of the ureter is extremely rare, and only 11 cases have been reported in Japan. This report describes a case of primary adenocarcinoma of the ureter we recently experienced.

CASE REPORT

The patient was a 66-year-old man. He consulted his family physician after observing gross hematuria, which was asymptomatic. Because of hydronephrosis observed on drip infusion pyelography (DIP), he was referred to our clinic on December 17, 2005. There was no past history or family history of note. Height and weight were 165 cm and 62 kg, respectively. No abdominal tumor mass or surface lymph node was palpable. The results of general blood analyses and blood biochemical analyses revealed no abnormal findings. Blood immunological tests were negative for prostate-specific antigen (PSA), carcinoembryogenic antigen (CEA), and carbohydrate antigen (CA) 19-9. In urinalysis, red blood cell count and white blood cell count were 4–5 and 1–2 per high power field, respectively, and urine cytology was negative. Left hydronephrosis was identified by ultrasonography of the kidney. Although the left renal pelvis was imaged on DIP, imaging of the ureter was poor, and retrograde pyelography (RP) was performed. RP showed stenosis of the left ureter at the L5 vertebral level. Antegrade pyelography, in combination with nephrostomy, confirmed the same observation as made by RP (Fig. 1). Adenocarcinoma was confirmed by biopsy using flexible pyeloscopy. Computed tomography showed a tumor in the middle of the left ureter (Fig. 2), but no metastasis was observed.



Fig. 1. Antegrade pyelography showed hydronephrosis and complete obstruction of the middle portion of the ureter.

Endoscopy showed no distinctive malignant lesions in the upper and lower digestive tract. From these observations, a primary adenocarcinoma of the ureter (T2, N0, M0) was diagnosed, and total left nephroureterectomy was performed on March 14, 2006. The dissected tissue weighed 375 g, and a pedunculated tumor of 15×10 mm was identified in the middle of the ureter (Fig. 3). Histopathological examination showed adenocarcinoma with growth of atypical columnar cells in glandular cavity form. There was infiltration to surrounding fat tissue through the muscle, while vascular infiltration was not observed (Fig. 4). Some carcinoma cells stained positive for CEA. Some cells stained positive for CK7 and CAM but not for PSA,



Fig. 2. Computed tomography using contrast medium demonstrated a suspicious mass (white arrow).



Fig. 3. Macroscopic findings showed a 15 × 10 mm non-papillary sessile tumor.

PAP, P501S, PSMA, CK20, CD31, and D2-40. From these results, we made the diagnosis of pT3, pN0, and M0 adenocarcinoma of the ureter. The patient is being followed as an outpatient without adjuvant therapy. No distinct recurrence or metastasis was observed on CT 6 months after surgery.

DISCUSSION

The tissue type of primary carcinoma of the

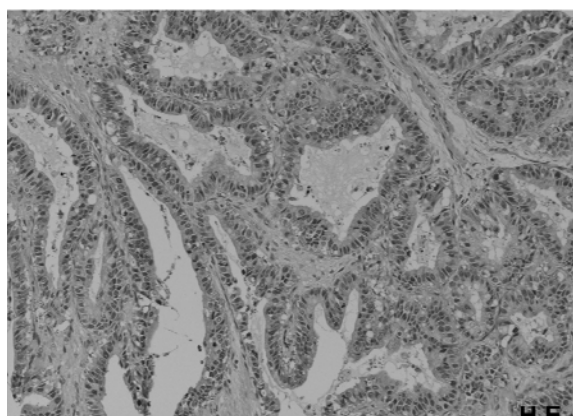


Fig. 4. H.E. and immunohistochemical staining. H.E. staining revealed adenocarcinoma with growth of atypical columnar cells in glandular cavity form.

pyeloureter is mostly transitional cell carcinoma and rarely adenocarcinoma. Transitional cell carcinoma, squamous cell carcinoma, and adenocarcinoma comprise more than 90%, 0.7–7%, and less than 1%, respectively, of cases¹⁾. Among them, primary adenocarcinoma of the ureter is extremely rare, and has been reported in only about 90 cases worldwide. In Japan, only one case has been reported³⁾ since the 10th report by Nasu et al.²⁾ in 1997. Our case is the 12th report in Japan. Table 1 shows the cases reported in Japan^{4,5)}. The onset age was 37–81 (mean : 62 years old), and there were 9 men and 3 women. The tumor developed on the right side in 9 cases and on the left in 3 cases. The major symptoms were hematuria, low back pain, abdominal pain and urinary disturbance. It was very rare that primary adenocarcinoma presented as asymptomatic hematuria, as in this case. In most cases, the diagnosis was made by pathological examination of the tumor after surgery, or the tumor was accidentally discovered after nephroureterectomy for other diseases such as urinary calculus or pyonephrosis. There have been only 2 cases, including this case, where adenocarcinoma of the ureter was diagnosed by biopsy before surgery. This could be because most cases were associated with urinary calculi

Table 1. Reports of primary adenocarcinoma of the ureter in Japan

No	Age/Sex	Laterality	Infection	Stone	Therapy	Prognosis
Nasu, et al. ²⁾	77F	R	—	—	Nephrectomy	Alive (6 months)
“	49M	R	Unknown	+	Nephroureterectomy	Unknown
“	69M	R	Unknown	—	Nephroureterectomy	Unknown
“	65M	R	+	+	Nephroureterectomy	Alive (6 months)
“	37M	R	+	—	Nephroureterectomy	Alive (1 year)
“	81M	R	+	—	None	Death (3months)
“	62F	R	—	—	Nephroureterectomy	Alive (3 months)
“	48F	L	+	—	Nephroureterectomy	Death (10 months)
“	64M	R	+	+	Ureterectomy	Alive (2 months)
“	55M	L	+	+	Nephrectomy	Alive (3 months)
Ohata, et al. ³⁾	80M	R	—	—	Nephroureterectomy	Alive (6 months)
Present case	66M	L	—	—	Nephroureterectomy	Alive (6 months)

or pyonephrosis, and the symptoms associated with ureteral tumors were masked by these complications, or surgery was performed without biopsy when a ureteral tumor was clearly indicated. However, when cytodiagnosis is negative, as in the present case, endoscopy is essential for making the diagnosis. If the tumor is small, endoscopic laser surgery, a less invasive procedure, can be performed. Although the mechanism of adenocarcinoma development in the urothelium remains controversial, epithelial metaplasia of the urinary mucosa is a widely accepted theory. Holly et al. suggested that metaplasia of the urinary mucosa takes two forms; squamous metaplasia which is an epidermal transformation, and glandular metaplasia which is an endodermal transformation, both of which can develop simultaneously⁶⁾. Anderson also suggested two processes of squamous and columnar epithelial metaplasia for urinary epithelial metaplasia⁷⁾. Considering the potential transformation of the urinary epithelium to squamous, columnar or cuboidal epithelium, Mostofi suggested two possible malignant transformations; one by columnar and squamous epithelial metaplasia, and the other in Brunn's nests and cystitis glandularis. Malignant transformation can be accelerated by chronic stimulation by calculi and chemicals, urinary infection, urinary disorder, radiation, and vitamin A deficiency⁸⁾. Since complications of calculus or urinary infection were noted in 7 out of 11 cases in Japan, these factors could be strongly correlated with malignant changes. In another hypothesis, adenocarcinoma was suggested to develop through metaplasia of transitional cell carcinoma itself. Furthermore, Arcadi suggested that calculus or chronic inflammation does not precede carcinogenesis, but that obstructive uropathy, induced by mucinous material produced by adenocarcinoma, results in calculus or chronic inflammation⁹⁾. Similarly, Linwnicz reported calculus formation due to obstruction from complex formation of cations with glycoprotein produced from mucinous cells¹⁰⁾. However, there are cases with an absence of calculus, inflammation and mucin production, including the present case. Therefore, the exact mechanism of adenocarcinoma development remains to be clarified. Regarding therapeutic choices, since radiotherapy is ineffective against adenocarcinoma, and

no effective chemotherapeutic regimen has been established, surgery is generally the treatment of choice, and total nephroureterectomy is performed in many cases, as in the present case. The long-term outcome is unknown in many cases reported in Japan, and a poor prognosis has generally been reported. Delayed discovery because of complications of calculus or inflammation, or the lack of effective adjuvant therapy could result in a poor outcome. Careful follow-up will be required in the present case because of infiltration of fat tissue by the tumor.

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和文抄録

原発性尿管腺癌の1例 : Primary adenocarcinoma of the ureter

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患者は66才, 男性. 無症候性肉眼的血尿を主訴に受診, DIP では左水腎症を認めたが尿管の抽出が不良であったため, retrograde pyelography (RP) を施行した. RP では, 第5腰椎レベルで左尿管の狭窄を認め, 腎瘻増設を兼ねて行った antegrade pyelography では RP と同様に, 第5腰椎レベルで狭窄を示していた. 同時に施行した軟性腎盂鏡では狭窄部位に一致して白色の

腫瘍を認めたため, 生検を施行した. 病理組織検査の結果は adenocarcinoma であった. 原発性尿管腺癌 (T2, N0, M0) の診断にて左腎尿管全摘除術を施行した. 本症例はわれわれが調べえた限りでは本邦12例目であった.

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