

Primary Adenocarcinoma of the Ureter with Elevated Carbohydrate Antigen-19-9: A Case Report and Review of the Literature

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Abstract

Primary adenocarcinoma of the upper tract urothelial cell carcinomas (UTUCs) is rarely reported. We report a case of primary adenocarcinoma of the ureter with elevated carbohydrate antigen 19-9 (CA-19-9). A 44-year-old male was admitted to the hospital for severe right flank and hypogastric pain for 7 days without visible or microscopic haematuria. The patient underwent radical nephroureterectomy followed by chemotherapy with gemcitabine/carboplatin and inorelbine/Adriamycin (ADM)/5-fluoro-2,4 (1 h, 3 h) pyrimidinedione (5-FU) and radiotherapy, and the level of CA19-9 decreased to normal. Histopathology revealed adenocarcinoma. The patient died of tumor pelvic metastasis after 6 months. A review of the literature is also reported.

Keywords: Adenocarcinoma; Upper tract urothelial cell carcinoma; Carbohydrate antigen 19-9

Abbreviations: EA: Carcinoembryonic Antigen; CA-19-9: Carbohydrate Antigen 19-9; CA125: Carbohydrate Antigen-125; UTUC: Upper Urinary Tract Urothelial Cell Carcinoma; U: Units; RNU: Radical Nephroureterectomy

Introduction

Urothelial carcinomas (UCs) have become the fourth most common cancer, and bladder cancer is the most common urinary tract carcinoma (about 90% to 95% of UCs). However, upper urinary tract urothelial cell carcinomas (UTUCs) are uncommon (only about 5% to 10% of UCs) [1,2]. Among UTUCs, urothelial tumors are more often observed, and squamous cell carcinoma of the upper urinary tract represents <10% of tumors and is even rarer within the ureter. Moreover, pure primary adenocarcinoma of the ureter is the rarest, accounting for <1% of all urothelial tumors [1]. Adenocarcinoma can be further subdivided into tubulovillous, mucinous, and papillary non-intestinal carcinoma. The first two groups included about 93% of the cases [3].

Since first adenocarcinoma of UTUC was described in 1946 by Ackerman [4], only about 100 cases have since been reported. Because tumors arising from the transitional epithelium seldom produce CA19-9, CEA or CA-125, so it is extremely rare that primary adenocarcinoma of UTUCs has elevated carbohydrate antigen-19-9 (CA-19-9), carcinoembryonic antigen (CEA) or carbohydrate antigen-125 (CA-125). Most reports revealed that the adenocarcinoma of UTUC usually occurred following glandular metaplasia of the transitional epithelium induced by chronic inflammation and urinary calculi. The present study reports a case of pure primary adenocarcinoma of the ureter with elevated CA-19-9. Literatures concerning the previously published cases are reviewed for a comprehensive study.

Case Presentation

A 44-year-old male without any medical history was admitted to the hospital for severe right flank and hypogastric pain for 7 days without visible or microscopic haematuria. At the time of admission, the patient's body temperature and blood pressure were 36.5°C and 140/89 mmHg, respectively. He was 63 inches tall, weighing 147 pounds, with a BMI of 25.8. The patient's condition was well, and weight loss, night sweats and recent fever did not present. And physical examinations showed slight right hypogastric tenderness. There was no significant surgical history and relevant family history mentioned. His routine hematological tests and urinalysis were within normal limits, and urine

culture was negative. However, CA-19-9 was 113.2 U/ml (normal range, <37 U/ml) with normal CEA (0.81 ng/ml; normal range, <5 ng/ml) and CA-125 (13.23 U/ml; normal range, <35 U/ml). The intravenous pyelography (IVP) showed no development of right renal pelvis. The computed tomography (CT) scan confirmed tumor-like lesion at lower ureter, possible metastasis of pelvic lymph nodes, hydronephrosis and hydroureter, and no calculi was found. Technetium-99 m diethylene-triamine-pentaacetic acid renal scintigraphy revealed an almost non-functioning right kidney. The retrograde pyelography revealed that ureteral catheter Foley-5 was blocked after entering ureter about 4 cm, and ioversol didn't develop the right ureter.

The diagnosis was tumor-like lesion at lower ureter. Subsequently, the patient underwent a radical nephroureterectomy. Intraoperatively, the appendix was swelling, so the appendectomy was performed. The gross pathological examination revealed the tumor in the ureter measured about 3.5 cm × 1 cm, and microscopic pathological report revealed low differentiated adenocarcinoma in ureter (Figure 1), and carcinomas were found at fibrous or adipose tissues of the pelvis and vena iliaca externa. Five lymph nodes around vena iliaca externa did not found carcinoma, appendicitis was detected (Figure 1). The tumor cells of Periodic Acid-Schiff (PAS) staining were positive (Figures 1A-1D), but lacked immunoreactivity for CD31, CD34, P504S and PSA.

The patient underwent chemotherapy and radiotherapy postoperatively. First, the patient underwent two cycles of 1.4 g gemcitabine and 500 mg carboplatin, then one cycle of vinorelbine, adriamycin (ADM) and 5-fluoro-2,4 (1 h, 3 h) pyrimidinedione (5-FU) (the dose was not in detail), then the patient showed I° myelosuppression and II° gastrointestinal tract reaction, 20 days later, he underwent the radiotherapy, the implantation of fourteen radioiodine-125 (¹²⁵I) particle was performed, the implantation site was around vena iliaca externa. Every particle had 0.6 mCi radioactivity, and CA-19-9 was decreased to

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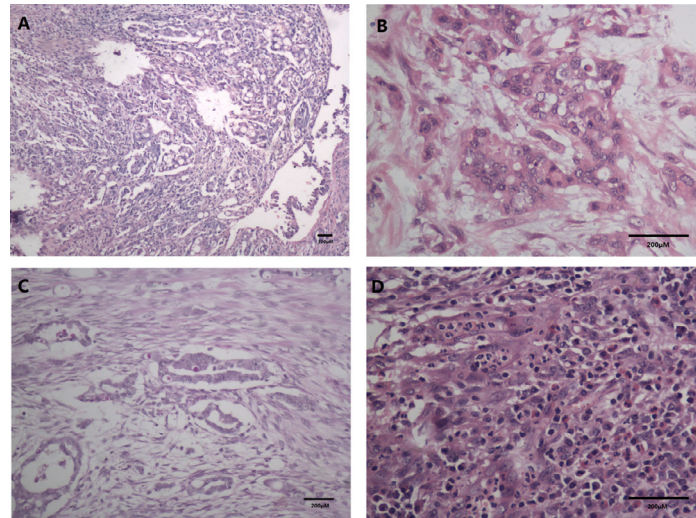


Figure 1: Pathological examinations of ureteral tumors and appendix (A) tumors in ureter are adenocarcinoma (hematoxylin-eosin, HE × 100) (B) Adenocarcinoma cells (HE × 400) (C) Periodic Acid-Schiff (PAS) stain in the tumour cells (× 200) (D) Appendicitis (HE × 400).

Author/Year	Year	Age	Sex	Site	Tumor marker	Treatment	Outcome
Iwaki [13]	1996	62	Male	Left ureter	CA-19-9, 88.7 U/ml	RNU	Alive, no sign of recurrence during 2-year follow-up
Aida [14]	2002	69	Female	Right ureter	CEA, 24.5 ng/ml	RNU	Alive, no sign of recurrence during 1-year follow-up.
					CA19-9, 313.3 U/ml		
Kato [15]	2009	72	Female	Right renal	CEA, 5250 ng/ml	Chemotherapy followed by right RNU	Alive, no sign of recurrence during 18-month follow-up.
				Pelvis and ureter para-aortic	CA19-9, 18310 U/ml		
				Lymph node	CA125, 1234 U/ml		
Shih [16]	2010	73	Female	Left renal pelvis and the upper ureter	CA125 103.80 U/ml CA19-9 151.9 U/ml	Nephrectomy and upper ureterectomy	Dead, 5 months after surgery
Ye [17]	2011	56	Female	Right renal pelvis	CEA, 103.94 ng/ml	RNU	Dead, 5 months after surgery
					CA19-9 138.35 U/ml		
Yang [18]	2013	66	Male	The lower part of the left ureter, left renal pelvis and para-aortic lymph node	CA19-9 2739.6 U/ml AFP 407.8 ng/ml	RNU and lymph node dissection	Alive, no sign of recurrence during 11-month follow-up.
Present study	2016	44	Male	Right ureter	CA-19-9 113.2 U/ml	Chemotherapy and radiotherapy followed by RNU	Dead, 6 months after surgery

Table 1: Reported cases of tumor markers (CEA, CA19-9, CA125) positive adenocarcinoma of UTUC.

12.94 U/ml (normal range, <39 U/ml). Two months later, the patient died because of tumor pelvic metastasis. The overall survival time was about 6 months.

Discussion

The major pathological type of UTUC is urothelial tumor, and adenocarcinoma, squamous cell carcinoma, small cell carcinoma and sarcoma are the special types. Among those tumors, primary adenocarcinoma is a very rare pathologic type, even rarer within the ureter. Between January 2008 and November 2016, only one operative patient of UTUC was diagnosed with adenocarcinoma among 676 patients who underwent surgery in Qilu hospital.

The most common origin of adenocarcinoma was from the gastrointestinal system, but this patient was diagnosed with adenocarcinoma originated at the urinary system. The adenocarcinoma in UTUC is highly lethal. The carcinogenesis is so far not clear. It has been reported to be associated with long-term inflammatory irritation supported by chronic infection, hydronephrosis or and urolithiasis [5,6] and these irritations were risk factors for adenocarcinoma, being

disclosed in half of all these tumors [7]. This should be distinguished with tuberculosis in urinary system [8]. It is difficult to define an accurate diagnosis of primary adenocarcinoma of the ureter preoperatively. The clinical and radiological presentations are usually non-specific. The clinical presentation has similarity with nephropylitis, such as pain in kidney region, positive urine erythrocyte or positive pycyte in urine [9]. The cases are mostly diagnosed by pathological examination postoperatively [10].

An elevated level of CA-19-9 and CEA was usually occurred in adenocarcinoma of some organs, such as colon and stomach. Raphael et al. [11] have proved that preoperative serum CEA and CA-19-9 levels may be helpful for the diagnosis and act as biomarkers for predicting prognosis and recurrence. Xiong et al. [12] reported that only about 100 cases had been reported in the English studies, such as PubMed, Elsevier, Embase, Springer and EBSCO. To our knowledge, only six studies [13-18] had reported elevated CEA and/or CA-19-9 in upper tract urinary adenocarcinoma in the English medical literature to date (Table 1). Iwaki et al. [13] first reported elevated CA-125 in primary ureter adenocarcinoma and the author suggested that CA-125 might

be a useful marker, especially when a nonpapillary invasive tumor is suspected. Kato et al. [15] explored that the regimen of paclitaxel/carboplatin (PCa) might be considered as a first choice for treating patients with metastatic adenocarcinoma of the urinary tract. Yang et al. [18] showed both elevated AFP and CA-125 in patients with tumor in left renal pelvis and ureter and with a swelling para-aortic lymph node. Chemotherapy with gemcitabine/carboplatin was initiated after surgery.

Conclusion

So far, there is no universally acknowledged regimen of chemotherapy/radiotherapy for primary metastatic adenocarcinoma of UTUCs. Onshi et al. [19] had reported patients underwent paclitaxel/carboplatin regimen were more effective and had less severe side-effects than those underwent the methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) chemotherapy. In this current case, the patient had elevated CA-19-9 but normal CEA and CA-125. And the patient adopted chemotherapy with gemcitabine/carboplatin and vinorelbine/ADM/5-FU and radiotherapy. Chemotherapy regimen in current study did not seem to be effective, but CA-19-9 decreased to normal level without elevated CEA.

Other studies [16,17] claimed that tumor markers, such as, CA-125, CA-19-9 and CEA could be served as prognostic factors in monitoring the effect of the chemotherapy and the signs of recurrence. Although the patient died with normal CA-19-9 and CEA in present study, we couldn't ignore the value of them. They might play an important role on planning of the therapeutic strategy and monitoring of disease recurrence and progression.

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