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: Carinoembryonic 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 upper 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) (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 hydrourerter, 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 isoversol 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 appendicectomy 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 ilicaca externa. Five lymph nodes around vena ilicaca 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 II myelosuppression and II° gastrointestinal tract reaction, 20 days later, he underwent the radiotherapy, the implantation of fourteen radioiodine-125 (I125) particle was performed, the implantation site was around vena ilicaca externa. Every particle had 0.6 mci radioactivity, and CA-19-9 was decreased to

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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 nephropyelitis, 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 have been involved in the carcinogenesis of this patient. The results of elevated CA-125 in the patients with primary adenocarcinoma of the ureter in the present study were consistent with that of Iwaki et al. [13].

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.

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.

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) stainin in the tumour cells (× 200) (D) Appendicitis (HE × 400).
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. Onishi 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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