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

Jianfeng Cui*, Qiyu Bo*, Shouzhen Chen¹, Zhaocun Zhang¹, Yan Li¹ and Benkang Shi**

¹Department of Urology, Qilu Hospital of Shandong University, 107#, Wenhua Xi Road, Jinan, 250012 P.R. China
²Department of First Operating Room, Qilu Hospital of Shandong University, 107#, Wenhua Xi Road, Jinan, 250012 P.R. China

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 hypogastrum 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 CA-19-9 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 CA-19-9, CEA or CA-125, it is extremely rare that primary adenocarcinoma of UTUCs is 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 glanular 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. Literature 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 hypogastrum 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 hypogastrum tenderness. There was no significant surgical history and relevant family history mentioned. His routine study reports a case of pure primary adenocarcinoma of the ureter with elevated Carbohydrate Antigen-19-9. A Case Report and Review of the Literature. J Clin Case Rep 7: 995. doi: 10.4172/2165-7920.1000995

Copyright: © 2017 Cui J, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
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

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

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Site</th>
<th>Tumor marker</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aida [14]</td>
<td>2002</td>
<td>69</td>
<td>Female</td>
<td>Right ureter</td>
<td>CEA, 24.5 ng/ml</td>
<td>RNU</td>
<td>Alive, no sign of recurrence during 1-year follow-up</td>
</tr>
<tr>
<td>Shih [16]</td>
<td>2010</td>
<td>73</td>
<td>Female</td>
<td>Left renal pelvis and the upper ureter</td>
<td>CA125 103.80 U/ml</td>
<td>Nephrectomy and upper ureterectomy</td>
<td>Dead, 5 months after surgery</td>
</tr>
<tr>
<td>Ye [17]</td>
<td>2011</td>
<td>56</td>
<td>Female</td>
<td>Right renal pelvis</td>
<td>CEA, 103.94 ng/ml</td>
<td>RNU</td>
<td>Dead, 5 months after surgery</td>
</tr>
<tr>
<td>Yang [18]</td>
<td>2013</td>
<td>66</td>
<td>Male</td>
<td>The lower part of the left ureter, left renal pelvis and para-aortic lymph node</td>
<td>CA19-9 2739.6 U/ml</td>
<td>RNU and lymph node dissection</td>
<td>Alive, no sign of recurrence during 11-month follow-up</td>
</tr>
<tr>
<td>Present study</td>
<td>2016</td>
<td>44</td>
<td>Male</td>
<td>Right ureter</td>
<td>CA-19-9 113.2 U/ml</td>
<td>Chemotherapy and radiotherapy followed by RNU</td>
<td>Dead, 6 months after surgery</td>
</tr>
</tbody>
</table>

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, hydropnephrosis 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 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...
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. Oshni et al. [19] 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.

**Acknowledgements**

This work was supported by the National Natural Science Foundation of China (Grant 81470987 and 81170702 to B. Shi), the Tai Shan Scholar Foundation to B. Shi, the Science and Technology Development Project of Shandong Province (Grant 2014GSF118054 to B. Shi), and Science Foundation of Qilu Hospital of Shandong University (Grant 2015QLMS28 to B. Shi).

**References**