腎結石に合併したCA125, CA19-9産生性腎盂乳頭状腺癌の1例

(CASE REPORT OF RENAL PELVIC ADENOCARCINOMA ASSOCIATED WITH A RENAL STONE THAT PRODUCED CARBOHYDRATE ANTIGEN 125 AND CARBOHYDRATE ANTIGEN 19-9)

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**Title:**
Case report of renal pelvic adenocarcinoma associated with a renal stone that produced carbohydrate antigen 125 and carbohydrate antigen 19-9

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**Key Words:**
renal pelvic adenocarcinoma, carbohydrate antigen 125, carbohydrate antigen 19-9, renal stone, paclitaxel

**Running title:**
Azumi, et al.: Renal pelvic adenocarcinoma, renal stone
Abstract

A 68-year-old man underwent left side simple nephrectomy for symptomatic severe hydronephrosis with decreased function due to renal stone. Because of severe adhesion around the kidney, the renal pelvic wall was torn during the operation. Pathological diagnosis was papillary adenocarcinoma of the renal pelvis with positive staining for carbohydrate antigen 125 (CA125) and carbohydrate antigen 19-9 (CA19-9). Retrospective analysis of preoperative blood sample showed a high level of CA125 and CA19-9. Four-cycle adjuvant chemotherapy with paclitaxel/carboplatin (TJ regimen) was performed. However, local recurrence developed 1 month after the termination of chemotherapy. Although papillary adenocarcinoma of the renal pelvis is extremely rare, the possibility of renal pelvic tumor should be kept in mind for patients who have long-standing renal stone and hydronephrosis with irregularity at the renal pelvic wall. CA125 and CA19-9 can be a useful marker for upper urinary tract tumor.
**Introduction**

Carbohydrate antigen 125 (CA125) and carbohydrate antigen 19-9 (CA19-9) are widely used as a tumor marker of gastrointestinal tract. While CA125 and CA19-9 are known to elevate in urinary tract tumor, there are a few reports of papillary adenocarcinoma producing CA125 and CA19-9. We report a case of renal pelvic adenocarcinoma associated with a renal stone that produced CA125 and CA19-9.

**Case report**

A 68-year-old man was referred to our hospital because of persistent left upper abdominal pain and body weight loss of 10kg for previous 1 month. He had been previously treated for left renal staghorn calculi in our hospital but lost to follow-up. Abdominal enhanced CT scan (Figure 1) revealed marked left hydronephrosis and renal stone. Retrospective re-evaluation of CT-scan did indicate the presence of irregular masses at the renal pelvic and calyceal walls (Figure 1). Percutaneous nephrostomy was already performed at the referring hospital, but the urine drainage was not good and the symptom did not improve. Under the diagnosis of pyonephrosis due to renal stone, nephrectomy by a flank incision was performed.
Because of severe adhesion around the kidney, the peritoneum was opened and the renal pelvic wall was torn during the operation, and cloudy urine together with tissue-like debris came out into the surgical field. Pathological diagnosis was well differentiated papillary adenocarcinoma of the renal pelvis (Figure 2A) not papillary urothelial carcinoma or papillary renal cell carcinoma. Immunohistochemical study revealed that the cytoplasm of the cancer cells stained positively for carcinoembryonic antigen (CEA), CA125 and CA19-9 (Figure 2B, C). Retrospective analysis of preoperative blood sample showed a high level of CA125 (69 unit/ml) and CA19-9 (752 unit/ml) but not CEA. Although there was no obvious distant metastasis, intraoperative implantation of tumor cells was highly suspected. Upon the informed consent, an adjuvant chemotherapy with 4 cycles of paclitaxel (175 mg/m²) and carboplatin (dose adjusted to an area under the curve of 5) (TJ regimen) was performed. Serum level of CA19-9 and CA125 once decreased to 45 unit/ml and 12 unit/ml, respectively. However, 1 month after the last cycle of chemotherapy, abdominal CT scan revealed a local recurrence of the tumor. Thereafter obstructive ileus developed due to tumor invasion, and serum level of CA19-9 and CA125 increased rapidly (553 unit/ml and 34 unit/ml, respectively). He has been receiving palliative treatment, and alive for 7 months after the last cycle of
Discussion

Papillary adenocarcinoma of the upper urinary tract is extremely rare and only five cases producing CA125, CA19-9 or CEA have been reported (Table 1).\textsuperscript{1-5} To our knowledge this is the sixth case of papillary adenocarcinoma of the upper urinary tract that showed production of CA125, CA19-9 or CEA.

Ward suggested that adenocarcinoma of the urinary tract may result from urothelial changes caused by urolithiasis and chronic inflammation causing cystic and glandular metaplasia.\textsuperscript{6} Some urothelial tumors show elevation of these tumor markers, but in most of the urothelial tumors these markers do not elevate and they can not be a reliable indicator for tumor screening. Some reports have stated that the higher level of these markers correlate with the higher histological grade.\textsuperscript{7-9} In these cases, measurement of these tumor markers may be useful to monitor the effect of chemotherapy and the state of the disease during follow-up. In the present case, tumor recurrence was associated with an elevation of CA125 and CA19-9.

Long-standing renal stone can be associated with upper
urinary tract tumor including squamous cell carcinoma. The possibility of upper urinary tract tumor should be kept in mind for patients who have long-standing renal stone and hydronephrosis with irregular masses around the renal pelvic wall.

There is no established regimen for chemotherapy for advanced primary adenocarcinoma of the urinary tract. Onishi et al. reported that M-VAC (methotrexate, vinblastine, doxorubicin, and cisplatin) regimen of chemotherapy for papillary adenocarcinoma was not effective, but four cycles of TJ regimen resulted in complete disappearance of the primary tumor in the ureter and paraaortic lymph node swelling without severe side effects.4 Sakata et al. reported a case of primary adenocarcinoma of the renal pelvis and ureter producing α-fetoprotein (AFP) that was treated effectively with paclitaxel, ifosfamide and cisplatin (TIP regimen).10 In the present case, 4 cycles of adjuvant chemotherapy with TJ regimen temporarily decreased serum level of CA125 and CA19-9, but could not prevent the local recurrence.
References


7) Nakatsu H, Kobayashi I, Onishi Y, et al.: ABO(H)blood group


Legends for Figures

**Figure 1** Abdominal enhanced CT-scan revealed marked left hydronephrosis with renal pelvic stone. Irregular multiple masses were seen at the renal pelvic and calyceal walls.

**Figure 2** A: Histopathological examination of the renal pelvic tumor showed well differentiated papillary adenocarcinoma (H-E, ×200). B: Immunohistochemical staining for CA125 showed cytoplasmic staining (×200). C: Immunohistochemical staining for CA19-9 showed cytoplasmic staining (×200).

**Table 1** Reported cases of tumor markers (CEA, CA19-9, and CA125) positive adenocarcinoma of the upper urinary tract.
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患者は68歳、男性。腎結石による腎機能低下を伴った症候性高度水腎症のため左腎摘出術が施行された。腎周囲の強度の癒着のため、術中腎盂壁が破れた。病理学的診断は腎盂乳頭状腺癌で、CA125、CA19-9に陽性所見を示した。術前の血液検体を調べたところCA125およびCA19-9が高値であることが明らかとなった。術後化学療法としてパクリタキセルとカルボプラチンを用いたTJ療法が4サイクル施行された。しかし化学療法終了1ヶ月後に局所再発した。腎盂乳頭状腺癌は極めて稀な疾患であるが、長期にわたる腎結石や腎盂壁の不整を伴った水腎症が認められ
た場合、腎盂腫瘍の可能性があることを忘れていはならないであろう。CA125およびCA19-9は上部尿路腫瘍の有用なマーカーになり得る。
Figure 2B

Figure 2C
Table 1. Reported cases of tumor markers (CEA, CA19-9, and CA125) positive adenocarcinoma of the upper urinary tract

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Site</th>
<th>Tumor markers</th>
<th>Treatment</th>
<th>Status</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Haitel et al. (1996)</td>
<td>68</td>
<td>M</td>
<td>Left ureter</td>
<td>CEA, unknown</td>
<td>OP</td>
<td>DOD</td>
<td>3Mo</td>
</tr>
<tr>
<td>2</td>
<td>Iwaki et al. (1996)</td>
<td>62</td>
<td>M</td>
<td>Left ureter</td>
<td>CA19-9, 88.7&lt;sup&gt;①&lt;/sup&gt;</td>
<td>OP</td>
<td>NED</td>
<td>24Mo</td>
</tr>
<tr>
<td>3</td>
<td>Aida et al. (2002)</td>
<td>62</td>
<td>F</td>
<td>Left ureter</td>
<td>CEA, 24.5&lt;sup&gt;②&lt;/sup&gt;</td>
<td>OP</td>
<td>NED</td>
<td>12Mo</td>
</tr>
<tr>
<td>4</td>
<td>Onishi (2005)</td>
<td>72</td>
<td>F</td>
<td>Right renal pelvis and ureter, para-aortic lymphonode</td>
<td>CEA, 5250&lt;sup&gt;②&lt;/sup&gt;</td>
<td>CT+OP</td>
<td>NED</td>
<td>12Mo</td>
</tr>
<tr>
<td>5</td>
<td>Kohori (2005)</td>
<td>76</td>
<td>F</td>
<td>Left renal pelvis</td>
<td>CA19-9, 155&lt;sup&gt;①&lt;/sup&gt;</td>
<td>RT+CT</td>
<td>DOD</td>
<td>19Mo</td>
</tr>
<tr>
<td>6</td>
<td>Our case (2006)</td>
<td>68</td>
<td>M</td>
<td>Left renal pelvis</td>
<td>CEA, 3.5&lt;sup&gt;②&lt;/sup&gt;</td>
<td>CT+OP</td>
<td>AWC</td>
<td>6Mo</td>
</tr>
</tbody>
</table>

CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CA125, carbohydrate antigen 125
①, unit/ml; ②, ng/ml; OP, operation; CT, chemotherapy; RT, radiation therapy
DOD, died of disease; NED, no evidence of disease; AWC, alive with cancer; months, Mo
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