Response of Recurrent Urachal Cancer to Gemcitabine and Cisplatin Therapy: A Case Report and Literature Review

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Abstract. Urachal cancer is a rare malignancy and the standard treatment is surgical resection. The prognosis of recurrent and metastatic urachal cancer is extremely poor because there is no established chemotherapy regimen. Here, the response of one patient with recurrent urachal cancer to combination chemotherapy of gemcitabine (GEM) and cisplatin (CDDP) (GC) is described. And the chemo- and radio-therapeutic regimens available for such patients are reviewed. A 67-year-old man diagnosed with stage IIIA urachal cancer underwent complete surgical resection. However, pelvic recurrence was detected on computed tomography (CT) 5 months after surgery. GC therapy was started immediately and resulted in a pronounced reduction in pelvic mass after three cycles. However, a follow-up CT scan taken 5 months later showed growth of the pelvic mass and new liver metastasis. He received GC therapy again, which resulted in reduction of the pelvic and liver metastatic masses after two cycles. However, the patient refused another course of GC therapy due to severe side-effects. Subsequent progression of the disease included spread in both regions, followed by death 16 months after recurrence. Various treatment strategies offer relatively long survival of patients with urachal cancer including those with recurrence and metastasis. Although further studies are necessary to determine its therapeutic efficacy, GC therapy may be a useful option in the treatment of urachal tumors, including recurrent tumours.

Urachal cancer is an uncommon neoplasm reported to account for less than 1% of all bladder carcinomas and 0.01% of all neoplasms in adults (1). Although its pathogenesis is not fully understood, adenocarcinoma is common and the majority of patients are males in the fifth and sixth decades of life (2). The main form of treatment for this cancer is partial (segmental) or radical cystectomy with en bloc resection of the median umbilical ligament up to the umbilicus (3). On the other hand, several reports have shown that chemotherapy and/or radiation therapy can induce objective anticancer efficacy at least in some cases (4, 5); however, there is no standard chemotherapeutic regimen. The prognosis of patients with urachal cancer is generally considered to be poor due to advanced disease stage at diagnosis and high frequency of recurrence after primary treatment. In particular, the outcome of patients with recurrent urachal cancer is extremely poor (6, 7). In this report, a case of recurrent urachal cancer with pelvic, liver and lymph node metastases treated successfully with a combination of cisplatin (CDDP) and gemcitabine (GEM) is described.

Case Report

A 67-year-old man was referred to our hospital with a one-month history of asymptomatic gross hematuria. The medical history included appendectomy at the age of 19 years. Physical examination revealed a soft supra-pelvic mass. Cystoscopy detected a non-papillary mass at the bladder dome, which was later diagnosed as adenocarcinoma by biopsy. Magnetic resonance imaging (MRI) and computed tomography (CT) scan (Figure 1A) revealed a 3x4 cm mass extending from the bladder dome to the median umbilical ligament. There were no abnormal findings regarding lymph nodes, other organs and bone, as confirmed by various imaging examinations. The mass was diagnosed as adenocarcinoma of urachal origin and radical cystectomy with urachal remnant resection was performed. The tumour was confirmed to be adenocarcinoma by histopathological examination (Figure 2). The cancer cells extended to the bladder, but spared the abdominal wall and peritoneum (stage IIIA urachal cancer according to Sheldon et al.’s classification (1)). Adjuvant therapy was not applied. Five months after surgery, a solid mass was detected behind the pubis (Figure 1B) together with lymph node involvement. Accordingly, the patient received three cycles of GEM and CDDP (GC)
therapy with (GEM 1,700 mg on days 1, 8, and 15; CDDP 120 mg on day 2 of each 28-day cycle). Completion of this chemotherapy resulted in a pronounced reduction in pelvic mass size (Figure 1C) and resolution of lymph node swelling. However, the patient suffered from severe nausea and fatigue despite treatment with various anti-emetic agents and steroids. Accordingly, he was treated with GEM only (at 1/4w) for 5 months by ambulatory care. After the completion of therapy, the CT scan showed enlargement of the pelvic mass and new liver metastases (Figure 1D and E, respectively). At that stage, the patient requested another course of GC therapy, and two cycles of a modified GC therapy (GEM 1600 mg on days 1 and 8; CDDP 110 mg on day 2 of each 28-day cycle) were provided. This resulted in a significant resolution of the pelvic and liver metastatic tumours (Figure 1F), as well as the metastatic liver mass (Figure 1G). Another cycle of GC therapy was recommended, but the patient refused due to the appearance of severe side-effects. Two months later, there was progression of the disease in both regions. In spite of combination chemotherapy of GEM and paclitaxel (1,000 mg and 100 mg, respectively on day 1 and 8 of each 28-day 3-cycle), the patient died 16 months after recurrence.
Local recurrence has been reported to occur in 15-18% of urachal carcinomas within the first 2 years of follow-up (3, 8). Similar to the primary tumour, the most effective treatment for recurrent urachal cancer is considered to be surgical resection. In fact, one study reported that after surgical resection, 4 out of 6 (66.7%) patients with local recurrence and no metastasis exhibited a 15-year cure (8). Reviewing the literature of studies on the prognosis of patients with local recurrence (pelvis, bladder, remnant) six studies (Table I) showed only four patients who underwent surgical resection and three of them had relatively long disease-free survival (23, 30 and 36 months). Thus, the most important factor for prolonged survival seems to be complete surgical resection of recurrent tumours (4, 9). On the other hand, the recurrence rates of distant metastasis are high (30-40%) (3, 8). The most commonly reported sites for distant metastasis are the liver, lymph nodes, lungs, and bones (3).

Actually, the current patient showed metastases in all of the aforementioned sites before death. Although prognosis is significantly affected by tumour stage, differentiation and histopathological type, advanced stage seemed to be the strongest predictor of poor prognosis (10, 11) and, patients with stage IV urachal cancer have extremely poor survival (6, 8). Thus, the management of metastatic tumours is important.

As shown in Table I, salvage surgery is often performed in patients with recurrent metastatic disease, but the role of surgery in the management of metastatic urachal cancer remains unclear. Some patients have received both surgery and another anticancer treatment modality, but a little information on the efficacy and long-term outcome was reported (8, 12). One patient with an isolated recurrent bone metastasis, treated with surgical resection only showed no metastatic disease at 6 months postoperatively, but no information on long-term outcome was presented (13). In general, data on the effect of surgical resection on prolongation of survival is limited in patients with multiple metastases. Various chemotherapeutic and radiation therapy regimens have been used in these patients (3, 6, 8). In one case (Table I), one radiomonootherapy irradiation focused on recurrent metastases in the ovaries, inguinal lymph nodes and acetabulum, and the patient remained alive with tumor at 6 months postoperatively (corresponding to 2 months after recurrence), but long-term survival and the effects of surgery were not reported. Thus, the clinical anticanter effect of radiation monotherapy for recurrent urachal tumor is speculated to be minimal. On the other hand, several reports have described the outcome of chemotherapy for metastasis and recurrent urachal cancer. The use of platinum-containing

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**Table I. Treatment and prognosis of patients with recurrent urachal cancer.**

<table>
<thead>
<tr>
<th>Recurrence site</th>
<th>Chemotherapeutic agent</th>
<th>Op/Rad</th>
<th>Outcome</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>LN, Bone</td>
<td>5-FU+MMC+MTX</td>
<td>No/Yes</td>
<td>Survival for 19 months</td>
<td>17</td>
</tr>
<tr>
<td>Local*</td>
<td>Intra-arterial 5-FU</td>
<td>Yes/No</td>
<td>No recurrence for 23 months</td>
<td>18</td>
</tr>
<tr>
<td>Bone</td>
<td>MVAC</td>
<td>No/Yes</td>
<td>Death after 15 months</td>
<td>7</td>
</tr>
<tr>
<td>Urethra</td>
<td>None</td>
<td>Yes/No</td>
<td>No recurrence for 15 months</td>
<td>19</td>
</tr>
<tr>
<td>Local*</td>
<td>MVAC</td>
<td>No/No</td>
<td>Symptom-free for 13 months</td>
<td>20</td>
</tr>
<tr>
<td>LN, Bone, Ovary</td>
<td>None</td>
<td>No/Yes</td>
<td>Alive with tumor for 2 months</td>
<td>21</td>
</tr>
<tr>
<td>Bone</td>
<td>None</td>
<td>Yes/No</td>
<td>Disease-free for 6 months</td>
<td>13</td>
</tr>
<tr>
<td>Local*, LN, Lung</td>
<td>S-1+CDDP</td>
<td>Yes/Yes</td>
<td>Disease-free for 30 months</td>
<td>22</td>
</tr>
<tr>
<td>Local*, Bone, Ovary</td>
<td>5-FU+LV+L-OHP¶</td>
<td>Yes/No</td>
<td>Death after 37 months</td>
<td>12</td>
</tr>
<tr>
<td>Lung</td>
<td>CPT-11</td>
<td>No/No</td>
<td>Reduced by 60%</td>
<td>23</td>
</tr>
<tr>
<td>Local*</td>
<td>IFX+TXL+CDDP</td>
<td>Yes/No</td>
<td>Disease-free for 36 months</td>
<td>3</td>
</tr>
<tr>
<td>Lung</td>
<td>None</td>
<td>Yes/No</td>
<td>Disease-free for 120 months</td>
<td>3</td>
</tr>
<tr>
<td>Local*</td>
<td>5-FU+CPT-11+LV</td>
<td>No/No</td>
<td>Disease-free for 6 months</td>
<td>24</td>
</tr>
<tr>
<td>Lung</td>
<td>DXR+MMC+CDPP</td>
<td>No/Yes</td>
<td>Disease-free for &gt;120 months</td>
<td>4</td>
</tr>
</tbody>
</table>

*Bladder, remnant, and/or pelvic tumor. ¶Followed by intraperitoneal hyperthermic chemotherapy (IPHC) with MMC. Op: operation after recurrence; Rad: radiation therapy after recurrence; MVAC: methotrexate+vinblastine+doxorubicin+CDPP; CDDP: cisplatin; LV: folinate; L-OHP: oxiliplatin; CPT-11: irinotecan; IFX: ifosfamide; TXL: paclitaxel; DXR: doxorubicin.

**Discussion**

Local recurrence has been reported to occur in 15-18% of urachal carcinomas within the first 2 years of follow-up (3, 8). Similar to the primary tumour, the most effective treatment for recurrent urachal cancer is considered to be surgical resection. In fact, one study reported that after surgical resection, 4 out of 6 (66.7%) patients with local recurrence and no metastasis exhibited a 15-year cure (8). Reviewing the literature of studies on the prognosis of patients with local recurrence (pelvis, bladder, remnant) six studies (Table I) showed only four patients who underwent surgical resection and three of them had relatively long disease-free survival (23, 30 and 36 months). Thus, the most important factor for prolonged survival seems to be complete surgical resection of recurrent tumours (4, 9). On the other hand, the recurrence rates of distant metastasis are high (30-40%) (3, 8). The most commonly reported sites for distant metastasis are the liver, lymph nodes, lungs, and bones (3).

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regimens produced stable disease or partial response in 71% of the patients (6). After salvage therapies including CDDP-based regimens in 29 patients with metastasis two of the patients were free of disease at the time of reporting after a follow-up period of over 4 years (8). Interestingly, one of these regimens was a combination of CDDP and GEM. However, details of the chemotherapeutic regimen, patients’ characteristics and course of progression were unfortunately not included. Thus, one cannot conclude that GC therapy suppresses the growth of all urachal carcinomas regardless of their malignant aggressiveness and behavior, especially since liver metastasis appeared after the first GC therapy in the present case. However, we speculate that GC-based chemotherapy has antitumor effects, at least in reducing tumour volume. Histopathologically, urachal adenocarcinoma are often described to be similar to gastric and colon adenocarcinomas. Chemotherapy regimens that include irinotecan have been reported to be efficacious for metastatic gastric and colorectal carcinoma (14, 15). In addition, colon cancer-specific FOLFOX-based chemotherapy has been used for metastatic urachal cancer with some success (12, 16). A single patient with urachal cancer who presented with multiple metastases was treated by en bloc resection of the urachus with partial cystectomy and lymphadenectomy, followed by adjuvant chemotherapy (CDDP, 5-FU, and DXR). DXR, and VP-16 as well as 5-FU, CDDP and interferon-α showed no evidence of disease for more than 11 years after the initial treatment (4). Thus, the use of a combination of various treatment modalities to improve prognosis and survival of patients with recurrent urachal cancer seems warranted.

In conclusion, GC therapy seems effective in reducing the incidence of recurrence of urachal cancer. In the absence of a standardized chemotherapeutic regimen various treatment strategies show some effectiveness in urachal cancer.

Conflict of Interest

All Authors declare no conflict of interest.

References


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