Case Report

Cisplatin and S-1 for urachal carcinoma: A single-institution case series

Tetsuya Urasaki,1 Yoichi Naito,1,2,3 Nobuaki Matsubara,1,4 Masaoki Sasaki,1 Takahiro Kogawa1,2 and Ako Hosono1,3

1Department of Breast and Medical Oncology, National Cancer Center Hospital East, 2Division of Experimental Therapeutics, Exploratory Oncology Research and Clinical Trial Center, National Cancer Center Hospital East, Chiba, 3Rare Cancer Center, National Cancer Center, Tokyo, and 4Department of Urology, National Cancer Center Hospital East, Chiba, Japan

Abstract

Introduction: Urachal carcinoma is a rare cancer, manifesting predominantly as adenocarcinoma, and could be treated with chemotherapy in patients with advanced or recurrent disease. However, any standard chemotherapy regimens are yet to be determined.

Case presentation: We retrospectively reviewed five patients with urachal adenocarcinoma treated with a potent first-line chemotherapy, cisplatin and S-1, between 2011 and 2014. Among the five patients, three were males. The median age at diagnosis was 61 years, ranging from 47 to 67. The most common symptom at their first visit was macroscopic hematuria. The best response was stable disease in four patients, which persisted for 7 months. Three patients experienced only one episode of grade 3 toxicity. Cisplatin and S-1 was well tolerated and safe.

Conclusion: The activity of cisplatin and S-1 is modest and more efficacious treatment is desired against urachal carcinoma.

Key words: chemotherapy, cisplatin, S-1, urachal carcinoma.

Keynote message

The combination of CDDP + S-1 is a potent first-line chemotherapy regimen for patients with advanced or recurrent urachal cancer. We reviewed the cases of five patients who received CDDP + S-1 chemotherapy. CDDP + S-1 confers modest activity in these patients.

Introduction

Urachal carcinoma is one of the rare malignancies because of its frequency of occurrence and poor results with clinical research. In locally advanced urachal carcinoma, curative surgical treatment is recommended. However, in the recurrent or metastatic disease, any standard chemotherapy regimens have not been established yet.

The 5-year survival rate of patients with urachal carcinoma is <50%, which is poorer than the average cancer survival rate;1,2 this is because no standard chemotherapy regimen is available for the patients thus far. Some groups have used CDDP-based chemotherapy regimens for bladder carcinoma, but both MVAC and GC regimens have been insufficient to control the malignancy,1,3 while ITP regimen for urothelial tracts showed that one of six patients with urachal carcinoma achieved CR.4 Meanwhile, the immunohistochemical profile of urachal adenocarcinoma is similar to that of colorectal adenocarcinoma; CK20 and CDX2 are usually positive in both types, while CK7 positivity is variable.5 Moreover, similar to colorectal adenocarcinoma, urachal adenocarcinoma could also have microsatellite instability and KRAS mutations.6 Currently, many clinical groups use the chemotherapy regimens for colon carcinomas in treating urachal carcinoma patients: IFL, modified FOLFOX6, and IRIS.7–9 Siefker-Radtke et al. have reported effective outcomes with several chemotherapy regimens including both 5-FU and CDDP.1

Correspondence: Yoichi Naito
M.D., Department of Breast and Medical Oncology, National Cancer Center Hospital East, 6-5-1 Kashiwanoha, Kashiwa City, Chiba 277-8577, Japan. Email: ynaito@east.ncc.go.jp

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Abbreviations & Acronyms
5-FU = 5-fluorouracil
CA = carbohydrate antigen
CDDP = cisplatin
CI = confidence interval
CR = complete response
EGFR = epidermal growth factor receptor
GC = gemcitabine and cisplatin
Gem-FLP = 5-FU, leucovorin, gemcitabine and cisplatin
IFEP = ifosfamide, 5-FU, etoposide, and cisplatin
IFL = irinotecan, 5-FU, and leucovorin
IRIS = irinotecan and S-1
ITP = ifosfamide, paclitaxel, and cisplatin
LN = lymph node
MVAC = methotrexate, vinblastine, adriamycin, and cisplatin
OS = overall survival
PD = progressive disease
PFS = progression-free survival
PR = partial response
SD = stable disease

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implemented a phase II trial of Gem-FLP originally for adenocarcinomas of the urothelial tract and urachal remnant.10,11 The IFEP regimen, originally for advanced bladder cancer, was also applied to patients with urachal carcinoma.12 It is essential that the S-1 plus CDDP combination chemotherapy is the standard first-line treatment for patients with advanced gastric cancer.13 Also, CDDP + S-1 chemotherapy regimen has been reported to have some presumptive advantage in patients with urachal adenocarcinoma.12,14 In the present study, we retrospectively analyzed the clinical outcomes of patients with urachal adenocarcinoma treated with CDDP + S-1 chemotherapy in our institution.

### Case presentation

This study was approved by the Institutional Review Board of the National Cancer Center of Japan. Patients were eligible if they had confirmed adenocarcinoma of urachal origin, as determined histologically and by imaging. We retrospectively reviewed five patients who had been treated with CDDP + S-1 first-line chemotherapy regimen in our institution from June 2011 to March 2014.

The dosage and administration schedule of S-1 + CDDP were according to that in a previous report.13 S-1, an oral 5-FU derivative consisting of tegafur, gimeracil, andoteracil potassium, was administered orally at a dose of 80 mg/m² per day for 21 consecutive days, followed by 14-day rest. CDDP was administered intravenously for over 2 h at a dose of 60 mg/m² per day on Day 8 of each cycle. Treatment was repeated every 35 days up to a maximum of six cycles or unless disease progression was observed.

The diagnosis of urachal carcinoma was based on the MD Anderson Cancer Center criteria.15 Clinical, laboratory, radiographic, therapeutic, and pathologic data for each individual were retrieved from medical records. Tumors were staged by both the Sheldon and Mayo staging systems.2,16 Imaging data were reviewed according to the Response Evaluation Criteria in Solid Tumors version 1.1 criteria,17 and classified as CR, PR, SD, or PD.

Toxicity was graded according to the Common Terminology Criteria for Adverse Events v4.0. All statistical assessments were performed using the statistical package IBM SPSS version 23.0 (SPSS Inc., Chicago, IL, USA).

### Cohort characteristics

Five patients with urachal adenocarcinoma received treatment with CDDP + S-1. Clinical characteristics of the patients are shown in Table 1.

### Response and patient outcomes

Case summaries of all five patients with urachal adenocarcinoma, treated with CDDP + S-1 chemotherapy, are shown in Table 2. Four patients achieved SD and the other had PD, while no patients achieved either CR or PR. Only one patient completed six cycles of CDDP + S-1 chemotherapy. The disease control rate (proportion of patients with best response of CR or PR or SD) was 80%. For PFS and OS, the survival curves were estimated using the Kaplan–Meier method. Our case series demonstrates a median PFS and OS were 7.0 months (95% CI 2.5, 11.5) and 22.4 months (95% CI 0.0, 45.6), respectively (Fig. 1).

### Toxicity

The adverse events are shown in Table 3. Of the five patients, three experienced one episode of grade 3 toxicity. There were no therapy-related deaths.

### Discussion

This study is a single-institution case series of patients with urachal adenocarcinoma treated with CDDP + S-1 chemotherapy.

The efficacy of CDDP + S-1 chemotherapy has been previously reported in a patient with recurrent urachal carcinoma.14 The combination of S-1 + CDDP has been considered one of the most promising chemotherapy regimens against urachal adenocarcinoma. In a recent study, CDDP + S-1 regimen showed that two of six patients with
Table 2  Case summaries of five patients with urachal carcinoma treated by CDDP + S-1 chemotherapy

| No. | Age/sex | Chief complaint        | Histology (adenocarcinoma) | Stage | Sheldon\textsuperscript{16}  | Mayo\textsuperscript{17} | Status    | Surgery                                                                 | Eastern Cooperative Oncology Group performance status | S-1/CDDP (cycles) | Best overall response |
|-----|---------|------------------------|----------------------------|-------|------------------------------|---------------------------|-----------|-------------------------------------------------------------------------|----------------------------------------------------------------|------------------|------------------------|
| 1   | 67/male | Macroscopic hematuria  | With signet-ring cell carcinoma (mucin-producing) | IIIA → IVB (LN, bone) | II → IV                     | Recurrent                  | En bloc segmental resection | 1                                                           | 2                              | SD                      |
| 2   | 63/male | Macroscopic hematuria  | Poorly differentiated       | IVA (LN) | III                          | Recurrent                  | En bloc segmental resection with pelvic lymph node dissection | 0                                                           | 4                              | SD                      |
| 3   | 53/male | Upper abdominal pain   | Well differentiated (mucin-producing) | IVB (LN, lung, liver) | IV                          | Advanced                   | Not performed (inoperable) | 0                                                           | 1                              | PD                      |
| 4   | 47/female | Micturition pain     | Well to moderately differentiated tubular (mucin-producing) | IIIA → IIIC (peritoneal dissemination) | II → IV                    | Recurrent                  | En bloc segmental resection with bilateral lymphadenectomy Excision of the recurrent tumors and abdominal wall reconstruction using a right anterolateral thigh flap | 0                                                           | 2                              | SD                      |
| 5   | 61/female | Macroscopic hematuria  | Well to moderately differentiated | IIIA → IVB | II → IV (lung) | Recurrent                  | Laparoscopic en bloc partial cystectomy with bilateral lymphadenectomy | 0                                                           | 6                              | SD                      |
urachal carcinoma achieved PR. To date, CDDP + S-1 did not show any obvious safety problems in patients with urachal carcinoma. The combination chemotherapy was also well tolerated in our study. Meanwhile, our study showed modest outcome in urachal carcinoma patients treated with CDDP + S-1 chemotherapy. The low response rate of our study suggests the necessity of more active treatment for urachal carcinoma. Currently, the molecular-targeted therapy has been employed widely across the tumor type. Such approach should be integrated into the treatment of urachal carcinoma. A recent report showed that a patient with metastatic wild-type KRAS urachal cancer responded well to cetuximab, a chimeric mouse-human monoclonal antibody targeting the human EGFR. In considering anti-EGFR antibody therapy, patients with urachal adenocarcinoma should be tested for the presence of KRAS and BRAF mutations prior to therapy.

The major limitations of our study include the retrospective design, the small study cohort derived from a single institution, and rarity of the disease. Larger sample sizes could help determine the feasibility of the chemotherapy regimen, but patients with rare tumors may show similar treatment responses.

In conclusion, we reviewed the cases of five patients with urachal adenocarcinoma who received CDDP + S-1 chemotherapy. CDDP + S-1 confers modest activity for patients with advanced or recurrent urachal carcinoma, as indicated from the findings of previous reports and our study. To improve outcomes for urachal carcinoma patients, more efficacious treatment will be needed in the future.

**Conflict of interest**

The authors declare no conflict of interest.

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