Case Report

Switching cisplatin to carboplatin in chemotherapy for metastatic penile cancer in a patient intolerant to cisplatin

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Abbreviations & Acronyms
5-FU = fluorouracil
CBDCA = carboplatin
CDDP = cisplatin
CT = computed tomography
PET-CT = positron emission tomography-computed tomography
PTX = paclitaxel
SCC = squamous cell carcinoma

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Introduction: Cisplatin is currently the key drug in the chemotherapy regimen for metastatic penile cancer. There are few reports of alternative medicines for patients who cannot tolerate cisplatin. This report describes a case in which carboplatin was used instead.

Case presentation: The patient presented with a chief complaint of edema in the groin area. On close examination, penile cancer (cT2-3N3M0 stage IV) with pelvic lymph node metastasis was diagnosed. He was started on chemotherapy with cisplatin (50 mg/m^2 on days 1 and 2), paclitaxel (120 mg/m^2 on day 1), and 5-fluorouracil (1000 mg/m^2 on days 2–5), but he developed acute kidney failure on the 12th day, thought to be caused by cisplatin. Cisplatin was changed to carboplatin, and chemotherapy was continued. He has received nine courses of chemotherapy and is doing well.

Conclusion: A case of penile cancer safely and effectively treated with chemotherapy using carboplatin was reported.

Key words: advanced penile cancer, carboplatin, chemotherapy, cisplatin unfit.

Keynote message

This study presents a case of transitioning from cisplatin to carboplatin for metastatic penile cancer treatment due to adverse effects. It highlights carboplatin's efficacy and tolerability. The findings propose carboplatin as a feasible, less toxic alternative in similar clinical scenarios.

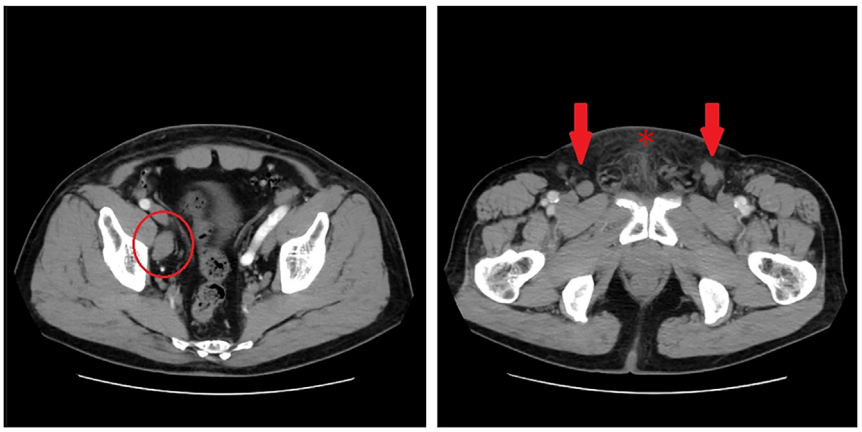
Case presentation

A 73-year-old Japanese man presented to our hospital with groin edema. The swelling had increased in the past 6 months, and he underwent a thorough examination at a nearby cardiology and urology clinic, but the cause of the swelling remained unknown. His height was 162 cm, and weight was 72.9 kg. He had a history of angina pectoris, cerebral infarction, and hypertension. He was taking bisoprolol, aspirin, cilostazol, febuxostat, rosuvastatin, nifedipine, and valsartan. On physical examination, there was edema of the entire penis because of which the glans were not visible. The scrotum to the perineum and pubic area was also edematous. Induration was present at the base of the penis but was not visible through the foreskin.

Radiographic imaging

CT showed edema of the perineum and lymphadenopathy in the pelvic and inguinal region (Fig. 1a,b).

On FDG-PET-CT, signal accumulation was observed at the root of the penis (Fig. 2) and the lymph nodes of the inguinal and perineal areas.



(a) (b)

Fig. 1 CT image of the pelvic region. (a) Circle: lymphadenopathy in the right obturator region, (b) Arrows: lymphadenopathy in the inguinal region. Asterisk: edema of the perineum region.

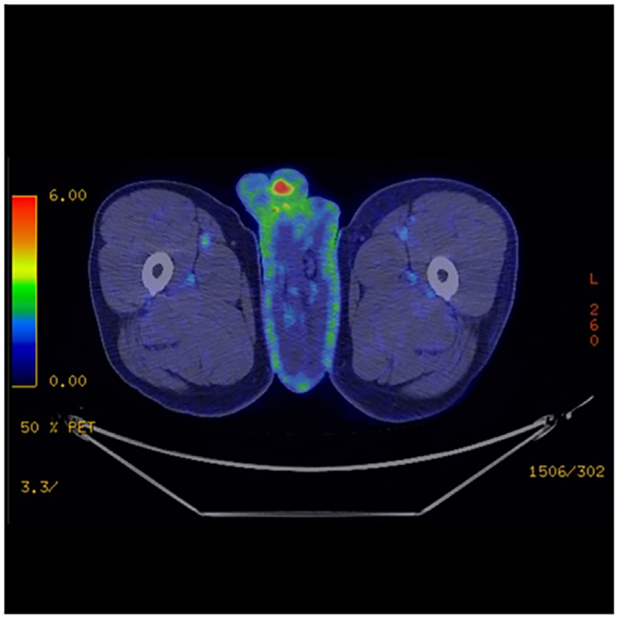


Fig. 2 FDG-PET CT image. Signal accumulation was observed at the root of the penis.

Clinical course

To confirm the diagnosis of penile cancer, lymph node excision in the inguinal region was performed by local anesthesia. Twenty-millimeter lymph node was removed from the body surface. Hematoxylin–eosin staining showed that metastatic tumors occupied the lymph node (Fig. 3a). In immunohistochemistry, the tumor was diffusely positive for cytokeratin (CK) 5/6 (Fig. 3b), CK34betaE12 (Fig. 3c), p63 (Fig. 3d), and p16 (Fig. 3e), which indicated SCC associated with HPV infection. The presence of HPV DNA was studied by using PCR (polymerase chain reaction with MY09/MY11 consensus primers targeting the L1 region of HPV). A band of 450 bp was observed (Fig. 3f), which corresponded to the predicted size amplicon. To determine the molecular identity, sequence analyses, and subsequent BLAST searching of the PCR amplicon were performed, and we identified it as HPV-16 type. Together with the results of images, penile cancer cT2-3N3M0 stage IV was diagnosed.

TPF therapy (50 mg/m^2 CDDP on days 1 and 2, 120 mg/m^2 PTX on day 1, 1000 mg/m^2 5-FU on days 2–5) was started 3 months after the initial visit. Pretreatment serum creatinine was 0.93 mg/dL, and eGFR was 61.5 mL/min/1.73 m^2. On the 12th day, acute renal failure (serum creatinine 4.65 mg/dL) was found, a nephrologist was consulted, and a diagnosis of nephrogenic renal failure caused by CDDP was made. Although renal function improved with drug withdrawal (serum creatinine 1.34 mg/dL), it did not recover to pretreatment normal values. It was determined that it would be difficult to continue the regimen with CDDP. In the literature, only regimens containing CDDP are recommended for penile cancer, with no articles on second-line therapy following CDDP failure. A decision was made to switch CDDP to CBDCA and continue the treatment regimen. Three months later, after the acute renal failure improved, chemotherapy (4 AUC CBDCA on day 1, 120 mg/m^2 PTX on day 1, and 1000 mg/m^2 5-FU on days 2–5) was started. As for side effects, grade 3–4 thrombocytopenia was observed until the sixth course, and each time, the thrombocytopenia resolved with conventional treatment. CT at this point showed that the patient was maintaining PR (Fig. 4).

CT at the end of the seventh course showed an increasing trend in inguinal lymph node size, and cancer genomic profiling tests were performed, but no genes that could be linked to treatment were identified. Clinical trials, including Phase I trials, were considered for participation, but none were available. After a discussion with the patient, it was decided to continue the current treatment because of his relatively good general condition and the maintenance of PR. The dose was reduced to 80% after the seventh course and continued every 2 months at intervals up to nine courses. The lymph nodes in the inguinal region have maintained PR but tend to increase, and the pelvic lymph nodes remain reduced in size. Surgical therapy is under consideration for more prolonged survival and a treatment-free period.

Discussion

SCC of the penis is a rare disease, accounting for 0.4%–0.6% of all malignant neoplasms among males in the United States and Europe.[1] No established standard of treatment has been

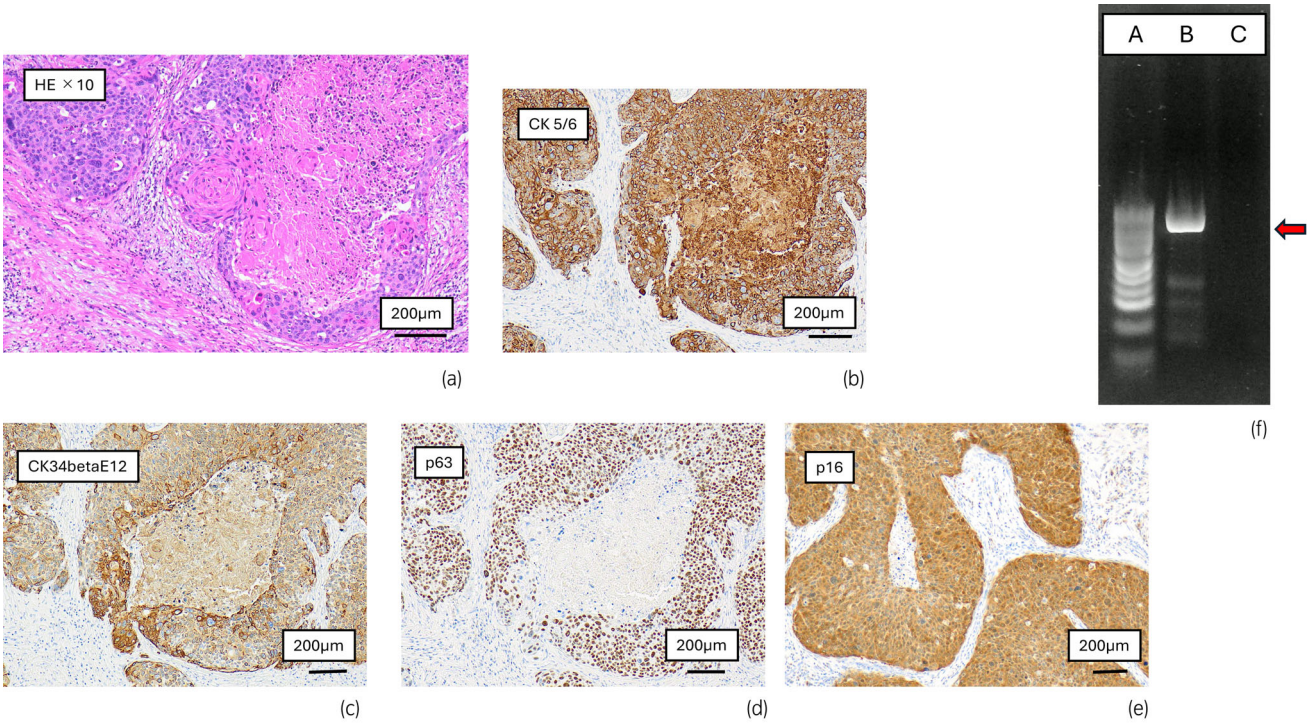


Fig. 3 Pathological findings. (a) Hematoxylin–eosin staining. (b–e) Results of immunohistochemistry. (b) cytokeratin (CK) 5/6, (c) CK34betaE12, (d) p63, (e) p16, (f) polymerase chain reaction (PCR) result. Lane A: size marker. Lane B: PCR product of sample DNA. Lane C: negative control. Arrow indicates 450 bp.

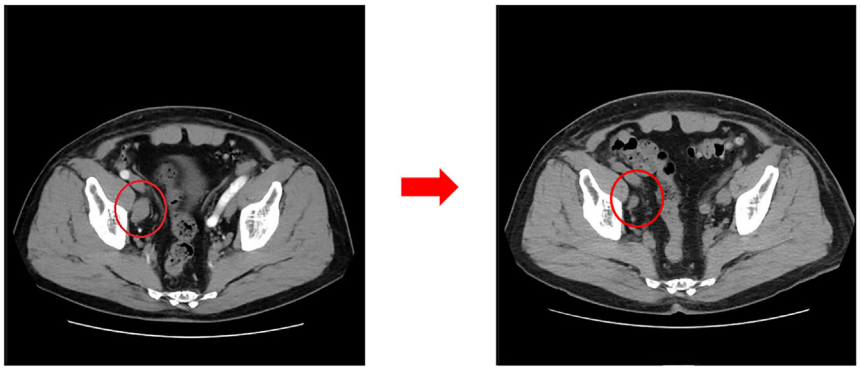


Fig. 4 CT images. Left: lymphadenopathy before chemotherapy. Right: lymph node shrinkage after six courses of chemotherapy.

confirmed by randomized controlled trials for metastatic penile cancer.[2] Combination chemotherapy has been reported more frequently than single-agent therapy.[3–7]

TPF therapy (PTX, CDDP, 5-FU) is a regimen reported in 2009 by Pizzocaro et al.[8] To date, two phase II TPF trials have been conducted.[9,10] TPF has been considered a relatively safe treatment. No adverse events of renal dysfunction were reported in these phase II studies.

However, at present, there has been no research on alternative regimens to CDDP in cases of CDDP failure or renal dysfunction. In urology, CBDCA has generally been used to replace CDDP in cases of CDDP failure in urothelial carcinoma, and its efficacy has been evaluated.[11] Regimens, including CBDCA, have become the standard of care for SCC, including esophageal cancers and head and neck cancers.[12,13]

Accordingly, CDDP was replaced by CBDCA in the general TPF regimen in the present case.

Eighteen months have passed since the initial diagnosis, and the patient continues to be treated and remains in good general condition, suggesting that the present treatment regimen has been effective. A case in which long-term disease control was achieved with the use of CBDCA, even though the patient could not tolerate CDDP. Although this is a single case report, the results of this report may not apply to all cases. Penile cancer is a rare carcinoma, and we hope to accumulate knowledge and improve treatment outcomes.

Author contributions

Keita Sekine: Conceptualization; data curation; writing – original draft. Takahito Suyama: Conceptualization; writing –

original draft. Kazuki Takei: Data curation. Hiroto Kato: Data curation. Ken Wakai: Validation. Atsushi Okato: Formal analysis. Kyokushin Hou: Validation. Kazuhiro Araki: Formal analysis. Kazuto Yamazaki: Data curation; writing – review and editing. Yukio Naya: Supervision; validation.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board and the approval number

Not applicable.

Informed consent

Informed consent was obtained from the patient for the presentation of the details of the case.

Registry and the Registration No. of the study/trial

Not applicable.

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