

Oncology

Syndrome of Inappropriate Secretion of Antidiuretic Hormone Caused by Carboplatin After Switching from Cisplatin in a Metastatic Urethral Cancer Patient



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ABSTRACT

There is no established chemotherapy regimen in metastatic primary urethral cancer (mPUC). The efficacy of a cisplatin (CDDP)-based regimen has been reported, however, when the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) occurs, the chemotherapy regimen should be changed to another platinum compound. In this report, we describe a 66-year-old woman who was diagnosed as mPUC with, CDDP-induced SIADH. After switching her to CBDCA and careful managing her sodium balance, three courses of the chemotherapy regimen were completed.

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Introduction

Primary urethral carcinoma (PUC) is an extremely rare malignancy. Recent reports described an annual incidence of 4.3 million in men, according to a review of databases from 1973 to 2002. In women, the incidence was about one-third higher than that in men. There is no established treatment for metastatic PUC (mPUC). Recent NCCN guidelines recommend that chemotherapy should be done based on the histology,¹ and in squamous cell carcinoma (SCC), which was most common in PUC, platinum-based chemotherapy should be performed in order to improve overall survival.²

During cisplatin-based chemotherapy, electrolyte abnormalities are common adverse effects that manifest regardless of primary site, and hyponatremia is the most common of them. Severe hyponatremia affects not only quality of life but may also be life threatening SIADH, which is symptomized by severe hyponatremia,

is characterized by water retention, central nervous system disorders, and pulmonary or endocrine disease. Cisplatin (CDDP) is associated with a higher incidence of SIADH than other platinum preparations, and some reports suggest that if CDDP-induced SIADH occurs, the regimen should be changed to another platinum compound.³ Nevertheless, no report has discussed the efficacy of switching from CDDP to carboplatin (CBDCA) after the emergence of SIADH. We report here on one case of severe CDDP-induced SIADH in a mPUC patient, in whom we managed the sodium balance and performed a total of 3 cycles of chemotherapy after switching to a CBDCA-based regimen.

Case presentation

A 66-year-old woman was admitted for investigation of continuous hematuria. Magnetic resonance imaging of the pelvis demonstrated a 40 × 36 mm multiseptated cystic mass replacing most of the pelvis (Fig. 1a, b), and transurethral biopsy of the vaginal mass revealed a squamous cell carcinoma. Computed tomography (CT) revealed bilateral inguinal lymph node metastases and multiple lung metastases, so the final diagnosis of the clinical stage was cT3N1M1. After informed consent, she received induction first-line chemotherapy, approved by the Institutional Review Board of Nagoya City University Hospital. The systemic chemotherapy

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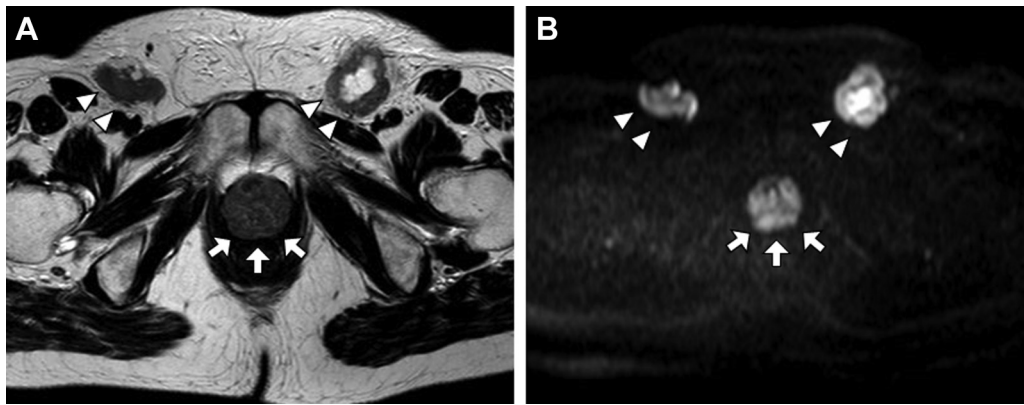


Figure 1. Magnetic resonance imaging of the pelvis. Urethral tumor (white arrow) and bilateral inguinal lymph node metastases (white arrowhead).

regimen was based on penile cancer; CDDP (25 mg/m² day 1–3), paclitaxel (PTX) (175 mg/m² day 1) and ifosfamide (1200 mg/m² day 1–3) were administered intravenously, and 4000 mL hydration per day was administered for 3 days in order to prevent toxicity. On day 4, she complained of moderate nausea and fatigue, and the symptoms worsened. On day 6, her serum sodium level was reduced to 101 mEq/L, the antidiuretic hormone (ADH) level was increased to 8.8 pg/mL (<4.2 pg/mL), and the plasma osmolality was 227 mOsm/kg, and urine osmolality was 492 mOsm/kg; the serum creatinine was 0.64 mg/dL, and the serum cortisol was 31.4 μg/dL (4.5–21.1 μg/dL) without edema or dehydration. She was diagnosed as CDDP-induced SIADH and treated with cautious hypertonic saline infusion. Her nausea was resolved and she recovered fully from fatigue. Her serum sodium level rose gradually to 133 mEq/L during 72 hours. She subsequently received 2 courses of a combination of PTX and ifosfamide without CDDP, which showed little efficacy against the metastatic lesions, supported by oral sodium and careful monitoring. SIADH did not recur, but the treatment was ineffective, and CT revealed progression of lung metastatic sites. She was received 3 courses of PTX and CBDCA as second-line chemotherapy, with continuous careful monitoring and sodium taken orally. After one complete cycle her serum

sodium level had decreased, and the ADH was increased; she was diagnosed as a relapse of SIADH on day 5 of the second cycle (Fig. 2), but it was controllable. In addition, grade 2 anorexia appeared as an adverse event, but it improved within 2 days. After 2 cycles of the second-line treatment the metastatic sites were stable, so one more cycle of the same regimen was administered. After completion of a total of 3 cycles of the PTX and CBDCA combination, her performance status worsened because of progression, and she died of cancer after palliative therapy for 2 months.

Discussion

SIADH is a disorder of impaired water excretion caused by an inability to suppress secretion of ADH. Some anticancer drugs may cause SIADH, in particular, CBDCA (Table 1) in combinations with PTX. In this case, SIADH occurred during first-line CDDP-based treatment, but the second and third cycles of treatment without CDDP did not cause hyponatremia. Uchida et al⁴ reported that CDDP induces SIADH by: (i) hyponatremia, which triggers increased renal salt reabsorption in order to reduce renal Na⁺ excretion in the loops of Henle, (ii) increased water re-absorption in the collecting ducts, which reduces the risk of nephrotoxicity, (iii) increased secretion of

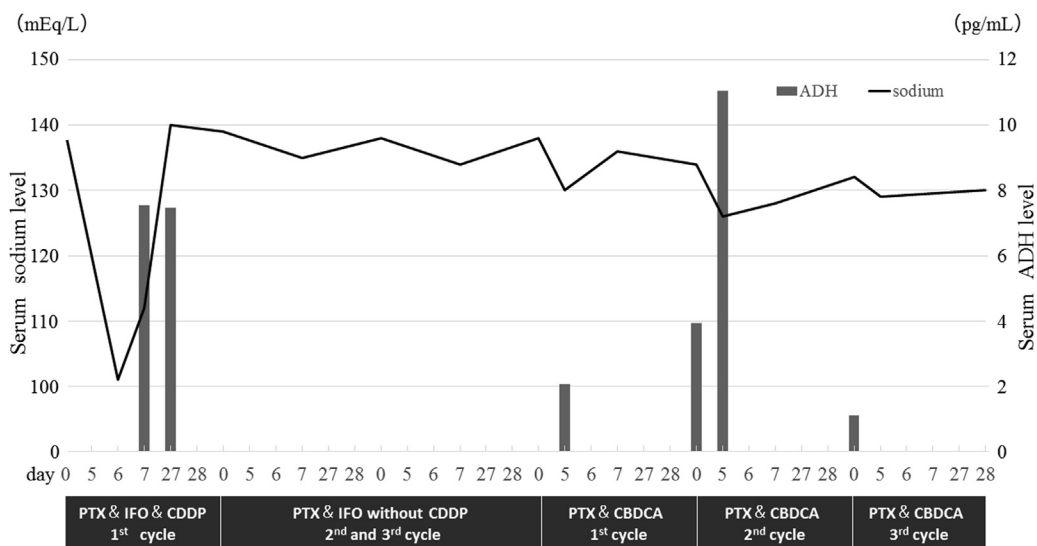


Figure 2. Serum sodium and antidiuretic hormone (ADH) level. Serum sodium level decreased to 101 mEq/L on day 6 of the first cycle of the initial chemotherapy. Serum ADH level was 8.8 pg/mL. Hyponatremia was improved by sodium supplementation, and then chemotherapy could be continued. During second-line chemotherapy, after completion of one cycle of the regimen, the patient's serum sodium level was again decreased and ADH increased, and she was diagnosed as relapse of SIADH on day 5 of the second cycle.

Table 1
Summary of articles on syndrome of inappropriate secretion of antidiuretic hormone (SIADH) caused by CBDCA

Age/Sex	Tumor Type	Chemotherapy Regimen	Onset of SIADH (Day After Injection of CBDCA)	Nadir Serum Sodium Level (mEq/mL)	Treatment
63/F	Adenocarcinoma in ovary	CBDCA + PTX	5	109	Unknown
60/F	Adenocarcinoma in lung	CBDCA + PTX	6	101	3% saline infusion
49/F	Breast cancer	CBDCA + DTX + trastuzumab	6	105	Fluid restriction
71/F	Adenocarcinoma in lung	CBDCA + PEM	7	118	Saline infusion (dose unknown)
Current case	Squamous cell carcinoma in urethra	CBDCA + PTx + ifosfamide	4	101	3% saline infusion

CBDCA, carboplatin; DTX, docetaxel; PEM, pemetrexed; PTX, paclitaxel; SIADH, syndrome of inappropriate secretion of antidiuretic hormone.

ADH induced by vomiting and pain. It was reported that CDDP-induced SIADH 4–6 days after start of treatment, and CBDCA caused SIADH within a similar time frame (Table 1). Therefore, during administration of the combination regimen, PTX and CBDCA, serum sodium levels should be monitored from the beginning treatment.

The pathogenesis of CBDCA-induced SIADH is unknown. Kagawa et al⁵ reported a successful completion of treatment with a combination of CBDCA and vindesine after switching from the regimen containing CDDP and vindesine in a lung cancer patient. The cases discussed here posed a high risk to the renal function partly because several of them needed a urinary diversion or a functioning solitary kidney. In urethral cancer, as in our case, it is not possible to switch from cisplatin even when electrolyte abnormalities occur, so switching to CBDCA from CDDP might be an option.

Conclusion

We experienced a case of severe SIADH caused by CDDP in a mPUC patient. Switching to a CBDCA-based regimen might be a feasible option in very rare urological malignancies.

Conflict of interest

There are no potential conflicts of interest.

Acknowledgments

None.

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