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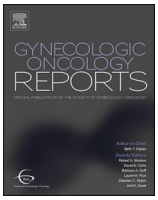

Case report

A case of hyponatremia attributed to carboplatin-induced syndrome of inappropriate anti-diuretic hormone

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1. Introduction

Syndrome of inappropriate antidiuretic hormone (SIADH) is a disorder in which inappropriate secretion of antidiuretic hormone (ADH) causes hyponatremia (Yasir and Mechanic, 2022). It has been reported that some patients develop SIADH during platinum drug use (Fujitsuka et al., 2022), with carboplatin reported to cause hyponatremia significantly less frequently than cisplatin (Ezoe et al., 2018). There is no clear recommendation regarding measures that should be taken in cases of carboplatin-induced SIADH. Here, we report a case in which carboplatin-induced SIADH was ameliorated via daily salt administration, allowing for the continuation of carboplatin therapy.

2. Case presentation

A 77-year-old woman with a history of myocardial infarction visited her physician due to abdominal distention. The patient was referred to our hospital after abdominal ultrasonography that revealed large volume of ascites. Paracentesis showed cytology consistent with adenocarcinoma. Magnetic resonance imaging (MRI) performed at our hospital showed a mass measuring 10 cm in diameter suspected to be ovarian cancer and tumor invasion of the bladder. There was no evidence of lymph node metastasis or peritoneal dissemination.

Open hysterectomy, bilateral adnexectomy, peritonectomy, and partial bladder resection were performed. Intraoperative findings showed that the anterior wall of the uterus had firmly adhered to the bladder. Surgery was completed without leaving any residual lesions. Postoperative pathology revealed ovarian cancer stage 1C3 (endometrioid carcinoma grade 1) without a bladder tumor. The patient was treated with paclitaxel-carboplatin (TC) combined chemotherapy (paclitaxel: 175 mg/m^2, carboplatin: area under the curve 6). Specifically, 220 mg paclitaxel and 440 mg carboplatin were used; dosages were calculated based on the patient's weight and renal function. Two days before the initiation of chemotherapy, blood tests revealed a normal serum sodium level of 138 mEq/L.

Six days after chemotherapy, the patient presented to the emergency department with fatigue. Vital signs were as follows: blood pressure (BP), 121/71 mmHg; heart rate (HR), 93 bpm; oxygen saturation of peripheral artery (SpO_2), 100% (room air); and body temperature (BT), 37.1 °C. Laboratory findings are shown in Table 1. Blood test findings revealed a serum sodium level of 121 mEq/L (less than the reference value of 135 mEq/L) and hyponatremia. Other test results were as follows: serum osmolality of 249 mOsm/kg (less than the reference value of 275 mOsm/kg), urinary sodium level of 153 mEq/L (more than the reference value of 40 mEq/L), and urine osmolality of 562 mOsm/kg (more than the reference value of 100 mOsm/kg). Since the patient had normal thyroid and adrenal hormone levels, normal skin turgor, and no fluid-restriction, the syndrome fulfilled the Schwartz and Bartter Clinical Criterion (Yasir and Mechanic, 2022), a commonly used clinical criterion for SIADH. The Schwartz and Bartter Clinical Criterion is used as the reference standard. The treatment strategy was as follows. Since the patient had no neurological symptoms or severe hyponatremia <

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Table 1
Laboratory test results of the patient at admission.

Laboratory test	Result	Reference range
Blood test		
White blood cell count (number/μL)	6,470	3900–9800
Hemoglobin (g/dL)	14.3	11.1–15.1
Platelet (number/μL)	87,000	130000–370000
Sodium (mmol/L)	121	137–144
Potassium (mmol/L)	4.2	3.6–4.8
Creatinine (mg/dL)	0.56	0.47–0.79
Blood urea nitrogen (mg/dL)	20	6.0–22
Glucose (mg/dl)	120	70–109
Serum osmolarity (mOsm/kg)	249	275–290
Argininr vasopressin (pg/mL)	0.5	< 2.8
Thyroid stimulating hormone (μU/mL)	3.93	0.5–5.0
Free throxine (ng/dL)	1.61	0.9–1.7
Adrenocorticotropic hormone (pg/mL	19.2	7.2–63.3
Cortisol (μg/dL)	19.4	3.7–19.4
Aldosterone (pg/mL)	95	30–159
Urine test		
Specific gravity	1.015	1.005–1.030
Sodium (mEq/L)	153	80–250
Creatinine (mg/dL)	40	22–328
Osmolality (mOsm/kg)	562	70–900

120 mEq/L, saline was administered rather than hypertonic saline while drinking water was restricted. KCL was also administered to prevent hypokalemia that could occur during treatment. The patient was admitted to the hospital and treatment with 1500 mL/day normal saline and 20 mEq daily KCL was initiated. Drinking water was also restricted to ≤ 700 mL per day. On day 6 post-admission, her serum sodium level improved to 134 mEq/L. The patient was discharged on day 7 of hospitalization.

Since TC therapy is an important ovarian cancer treatment, the possibility of continuing TC was discussed with the internal medicine department. The patient underwent a second round of TC therapy. On the same day, the patient's serum sodium level was 138 mEq/L. Three days later, blood was drawn, and the serum sodium level had decreased to 133 mEq/L. In contrast, her urinary sodium level was slightly elevated (45 mEq/L). Since the patient was at risk of becoming hyponatremic again if the condition persisted, a 2 g/day salt regimen was initiated. Two days later, her serum sodium level increased to 137 mEq/L (Table 2). Therefore, it was determined that continued oral salt administration would prevent hyponatremia. The patient continued taking 2 g/day of salt until the 14th day following TC therapy. Consequently, hyponatremia was avoided, allowing the patient to undergo a third round of TC therapy. Due to the success of salt therapy for preventing hyponatremia, the patient was able to receive six cycles of TC therapy, as scheduled. On the last follow-up, the patient was in remission from the first diagnosis.

3. Discussion

In the present case, the patient's thyroid and adrenal functioning was normal, suggesting a drug-induced cause of SIADH. Taxanes rarely cause hyponatremia (Neuzillet et al., 2016), while platinum drugs have been reported to cause the condition. Therefore, carboplatin was determined to have caused SIADH, although the frequency of hyponatremia development has been reported to be significantly low (Ezoe et al., 2018).

The ideal treatment strategy for patients with ovarian cancer who develop carboplatin-induced SIADH is unclear. Carboplatin is an important standard primary therapy for ovarian cancer (Pokhriyal et al., 2019); therefore, its continued use after the development of SIADH is warranted. Ideally, carboplatin should be continued even after SIADH development. In this case, by taking 2 g/day salt from the start of chemotherapy until day 14 following TC completion and performing regular blood tests, a total of six rounds of TC treatment was administered, as planned, while controlling SIADH. In patients who develop SIADH due to carboplatin, management of symptoms via salt administration allows for the continuation of cancer treatment, an insight with the potential to improve patient outcomes.

Table 2
Sodium levels on days 0–6 post-initiation of TC therapy.

Sodium (mmol/L)	Day 6	Day 7	Day 8	Day 9	Day 10
TC (first)	121	122	127	132	134
	Day 0	Day 3	Day 5		
TC (second)	138	133	137		

4. Conclusion

Even in patients with ovarian cancer who develop carboplatin-induced SIADH, it may be possible to continue carboplatin therapy in patients administered daily oral salt.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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