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Massive postoperative polyuria following total gastrectomy for gastric cancer

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Abstract
Massive postoperative polyuria is rare, except in neurosurgery patients. Here we report excessive polyuria in a 59-year-old woman following total gastrectomy for advanced gastric cancer. The etiology of the patient's polyuria was unknown. Urine output was measured hourly and replaced with Ringer's lactate solution at 80% of measured volume. The rate of urine output during 9 postoperative days ranged from 900 to 2700 ml·h^{-1}. Several administrations of an antidiuretic hormone (ADH) analogue were ineffective in reducing urine output, suggesting a possible relationship of the massive polyuria to nephrogenic diabetes insipidus. Following oral administration of a thiazide diuretic, known to exert an antidiuretic action in nephrogenic diabetes insipidus, urine output was dramatically reduced. We conclude that this case of massive polyuria probably resulted from postoperative nephrogenic diabetes insipidus.

Key words Polyuria · Nephrogenic diabetes insipidus · Postoperative

Introduction

The term polyuria refers to the production of abnormally large volumes of dilute urine. Patients diagnosed with polyuria produce more than 3 l of urine per day. Severe cases of polyuria encountered postoperatively are rare, except in cases of neurosurgery, such as resectioning of the pituitary gland; in these cases, the urine output is usually 300–500 ml·h^{-1}. Vasopressin can be used as an effective agent for reducing urine output in most cases. To date, there have only been a few reports of polyuria following abdominal surgery [1–3]. Some of these cases are nephrogenic diabetes insipidus, which is characterized by excessive volumes of dilute urine caused by the insensitivity of the distal nephron to the antidiuretic effect of arginine vasopressin. Here, we report on a case of massive postoperative polyuria that occurred after total gastrectomy and discuss the possible etiology of this case. We place particular emphasis on the time course of the urine output and serum chemical parameters.

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Case report

A 59-year-old woman was admitted to Kanto Rosai Hospital with epigastralgia that had persisted for several weeks. This patient had no previous medical history of diabetes mellitus and had never been treated with lithium, demeclocycline, diphenylhydantoin, propoxyphene, or amphotericin. Gastric fiberscopy revealed an irregularly shaped depressed lesion in the upper gastric body. Biopsy of the lesion revealed signet ring cell carcinoma. A complete blood cell count and chemical test results were within the normal range. Hemoglobin A1c was 5.4% (normal range, 3.6%–5.8%) and creatinine clearance was 46.4 ml·min^{-1}. Surgery for gastric cancer was performed 21 days after admission. Anesthesia was induced using 120 mg propofol, and tracheal intubation was facilitated by 6 mg vecuronium. Anesthesia was maintained with 1 l·min^{-1} O_2, 3 l·min^{-1} air, 0.5%–2.0% sevoflurane, and intermittent epidural injections of 1% mepivacaine. Total gastrectomy and splenectomy with a D2 lymph node dissection were performed. Blood pressure, heart rate, and other parameters were stable throughout the operation. During the 4 h of surgery, the patient excreted 300 ml urine and received 1950 ml Ringer's solution and 100 ml normal saline with 2 g cefazolin. Total intraoperative blood loss was 180 g. Immediately after the operation, the patient's blood pressure was 150/90 mmHg, heart rate was 80 beats·min^{-1},

respiratory rate was 18 min^{-1}, and core body temperature was 34°C.

Postoperatively, fluid was intravenously infused at 100 $ml \cdot h^{-1}$ and the urine output was 80–100 $ml \cdot h^{-1}$ for the first 12 h. The patient complained of thirst 15 h after the operation, indicating extracellular fluid depletion, and the urine output gradually increased to 200 $ml \cdot h^{-1}$. Intravenous fluid infusion did not improve the symptoms, and the urine output had increased to 300 $ml \cdot h^{-1}$ by 21 h after the operation. To rule out central diabetes insipidus, which is often associated with massive polyuria, 5 µg of the antidiuretic desmopressin acetate was sprayed into the nasal cavity three times; however, the urine output did not decrease. Nonsteroidal anti-inflammatory drugs, which are often used for nephrogenic diabetes insipidus, also failed to reduce the urine output. On the second postoperative day, the urine output had increased to 34.5 $l \cdot day^{-1}$. Ten units of vasopressin were injected intravenously on four separate occasions, but this intervention also proved ineffective. Serum levels of hormonal markers were within normal limits, except for adrenocorticotropic hormone and cortisol. The plasma antidiuretic hormone level was 2.7 $pg \cdot ml^{-1}$ (normal range, 0.3–3.5), renin activity was 1.2 $ng \cdot ml^{-1} \cdot h^{-1}$ (normal range, 0.3–2.9), adrenocorticotropic hormone level was 110 $pg \cdot ml^{-1}$ (normal range, 9–52), aldosterone level was 100 $pg \cdot ml^{-1}$ (normal range, 29.9–159), and cortisol level was 27.2 $\mu g \cdot dl^{-1}$ (normal range, 4.0–18.3). Intravenous fluid infusion compensated for the dehydration caused by the excessive urine output; this was employed because of the unknown etiology of the polyuria and the prohibition of orally administered water intake due to the patient's gastrectomy status. The patient received glucose-free Ringer's lactate solution in proportion to the urine output in addition to the regularly infused maintenance solution of 2000 $ml \cdot day^{-1}$: lactated Ringer's solution at 80% of the volume of the hourly urine output was infused per hour, consecutively. Exogenous vasopressin was administered to reduce the urine output but this failed to control the polyuria. On the 7th postoperative day, the esophagojejunal anastomosis showed no signs of leakage, and fluid was given orally. Subsequently, 4 mg of the thiazide diuretic trichlormethiazide was administered orally.

Urine output had increased massively on the 8th postoperative day to 46.8 $l \cdot day^{-1}$, despite the oral administration of trichlormethiazide. However, on the 9th and 10th postoperative days, the urine output decreased markedly to 19.5 and 4.7 l, respectively (Fig. 1), and no subsequent intravenous fluid infusion was required. The urine output rate over the 9 postoperative days ranged from 900 to 2700 $ml \cdot h^{-1}$. The daily volumes of urine and intravenously infused solution during the polyuric period are shown in Fig. 1; the total urine output was 3001 and the total volume of infused solution was 257 l. During this period, blood pressure was stable and dopamine support was not required. Although the urinary concentration of sodium was higher than normal, the serum concentration of sodium never fell below 138 $mEq \cdot l^{-1}$ (Fig. 2). Urinary sodium and chloride concentrations showed similar trends, and creatinine and potassium varied in the same way, with an almost inverse relationship to urine output (Fig. 2). Urine osmolarity was lower than 300 $mOsm \cdot kg^{-1}$ during the polyuric period. Pathological examination of the resected gastric cancer showed massive serosal invasion with peritoneal dissemination, lymph node involvement, and no liver metastasis.

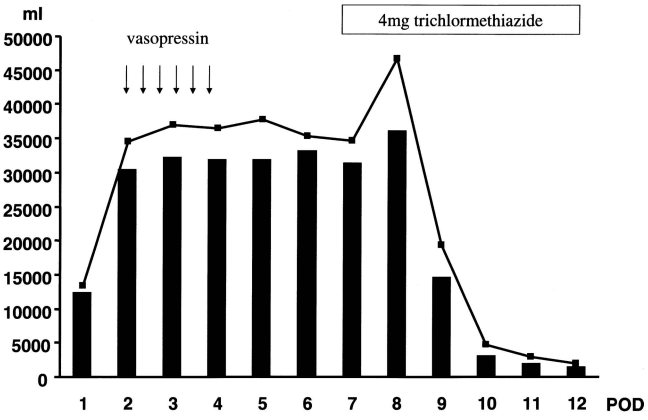

Fig. 1. Daily volumes of urine output and infused Ringer's lactate solution. *Dots* and *bars* indicate the daily volume of urine output and infused solution, respectively. Note that the volume of infused solution was smaller than the urine output each day. After the 8th postoperative day (*POD*), urine output dramatically decreased following trichlormethiazide administration

Discussion

This report describes an unusual case of massive postoperative polyuria after gastrectomy, in which the exact etiology remains unknown. Polyuria can be caused by inadequate secretion of vasopressin, failure of the renal tubules to respond to vasopressin, solute diuresis, natriuresis, or physiological adaptation to deliberate excessive water-drinking [4].

Solute diuresis and natriuresis are the most common causes of polyuria. Patients with diabetes mellitus often experience polyuria because of glycosuria, in which excess urine production acts as a mechanism for removing excess glucose from the blood. However, glycosuria was not observed in the patient described in this case, and there was no past history of diabetes mellitus. HbA1c levels were normal. In addition, glucose-free solution

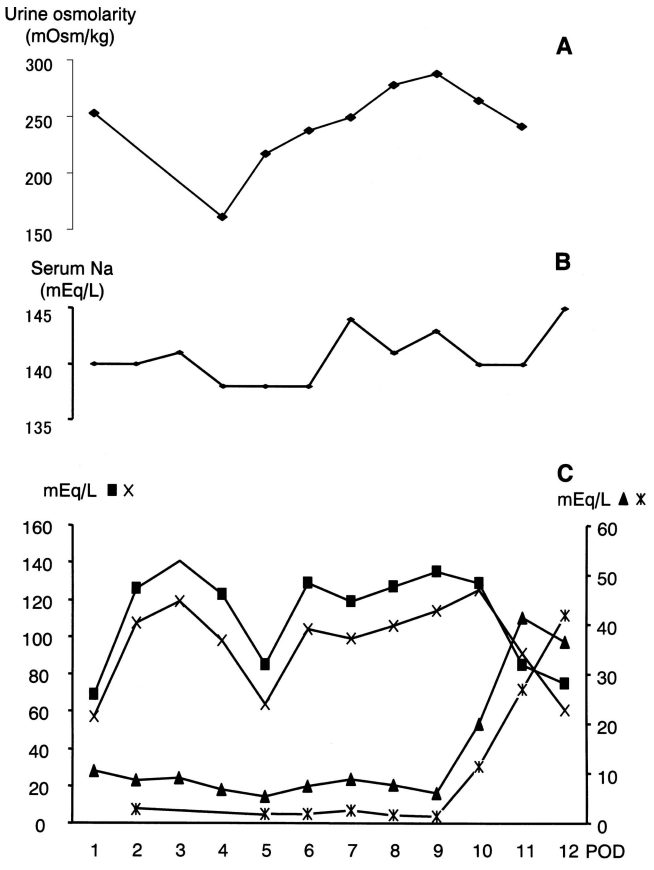

Fig. 2. Urine osmolarity (**A**), serum sodium concentration (**B**), and urinary variables (**C**), showing urinary sodium (*squares*), chloride (*crosses*), potassium (*triangles*), and creatinine (*asterisks*) concentrations. Urinary sodium did not decrease on the 9th and 10th postoperative days (*POD*) when the urine output was markedly decreased. Note that despite the massive urine output, serum sodium concentration was stable within the normal range. Urinary osmolarity was less than 300 mOsm·kg^{-1} during the polyuric period

was administered postoperatively in proportion to the urine output supplementally, and regular urinalyses for the presence of glucose were negative. Natriuresis might have contributed to the polyuria in this case, because high urinary sodium concentrations were observed; however, this was unlikely to be the main cause, as the serum sodium concentration never decreased significantly.

Polyuria is a common symptom of diabetes insipidus. In this case, central diabetes insipidus resulting from inadequate secretion of vasopressin was ruled out because the patient showed no response to exogenous vasopressin and the duration of the polyuria was short. Furthermore, serum antidiuretic hormone levels were in the normal range during the polyuric period. However, nephrogenic diabetes insipidus, which is a failure of the renal tubules to respond to vasopressin, appeared compatible with this case, as the administration of vasopressin was ineffective and produced no change in the urine volume.

Although the possibility of renal diabetes insipidus could not be excluded, the polyuria was too marked and transient to be explained solely in terms of common nephrogenic diabetes insipidus. This condition can be induced using several drugs, including lithium, demeclocycline, methoxyflurane, ethanol, diphenylhydantoin, propoxyphene, and amphotericin [5–12]. Our patient had never received any of these drugs; however, we could not exclude the possibility that peri- and postoperatively used drugs, such as cefazolin, sevoflurane, propofol, and mepivacaine, were causal with this polyuria. Most cases of drug-induced nephrogenic diabetes insipidus are reversible after the cessation of drug exposure, and the duration to reverse the polyuric symptoms was reported to be dependent on the length of drug exposure [5]. In our case, cefazolin was administered twice (before and after the operation; total, 4 g), and all the remaining drugs were used during the operation. Thus, it seemed unlikely that such a transient exposure of these drugs were the cause of polyuria for 9 days, although we did not confirm the symptoms after reintroduction of these drugs to exclude the causal relationship. Hypercalcemia is also among the causes of nephrogenic diabetes insipidus [13]. However, the serum calcium concentration was within the normal range during the polyuric period.

Thiazides and nonsteroidal antiinflammatory drugs are the most common treatment for nephrogenic diabetic insipidus. In this case, the antiinflammatory drugs used on postoperative day 1 did not decrease the urinary output; however, administration of trichlormethiazide on postoperative days 7 and 8 ameliorated the polyuric state, decreasing the urine volume almost immediately. Although thiazide diuretics are generally known to exert an antidiuretic action in nephrogenic diabetes insipidus [14], the exact mechanism behind this paradoxic antidiuretic response remains elusive. Janjua and colleagues reported that the antidiuretic response to thiazide administration could be explained by a reduction in the distal delivery of tubular fluid related to urinary sodium depletion [15]. Their in vivo study also showed that sodium replacement prevented thiazide-induced antidiuresis. In our patient, glucose-free Ringer's lactate solution containing 130 mEq·l^{-1} sodium was used in proportion to the urine output each hour. It is possible that, although this fluid replacement led to circulatory stability, the sodium replacement contributed to sustaining urinary sodium excretion and, thus, might have prevented a prompt antidiuretic response to trichlormethiazide.

To distinguish between primary polydipsia and diabetes insipidus, patients should generally undergo a water-deprivation test. However, our patient was prohibited

from taking water per os due to her post total gastrectomy status; therefore, deprivation of fluid administration was not an option in this unusual case. In addition, exogenously administered fluid did not exceed the urine output, which suggests that it is unlikely that the polyuria was caused by the primary polydipsia. Urinary osmolarity during the polyuric period never exceeded 300 $mOsm \cdot kg^{-1}$. The amount of administered fluid was unusually high, but it did not exceed the urine output. This finding indicates that the system regulating urine concentration was dysfunctional, suggesting that the primary polydipsia was not consistent with this case.

Recent studies have revealed that regulation of water reabsorption by antidiuretic hormone occurs in the principal cells of the collecting duct and is largely dependent on regulation of the aquaporine-2 water channel [16,17]. Aquaporin-2 is usually localized in cytosolic vesicles, and its function is mediated by cAMP-dependent translocation to the cell-surface membrane of epithelial cells in the collecting duct. In this case, no data were available concerning aquaporine-2. However, it is possible that some unknown mechanism triggered by surgical and/or anesthetic stress might have affected this cAMP-dependent pathway of the water regulatory system and transiently inhibited water reabsorption in the renal collecting duct.

In summary, we have presented a case of massive postoperative polyuria caused by nephrogenic diabetes insipidus. Although the exact etiology is unknown, oral administration of trichlormethiazide was effective in controlling the polyuria. Regulation of the water and electrolyte balance was essential for the management of this patient during the polyuric period, although sodium replacement might prevent the antidiuretic effect of trichlormethiazide in nephrogenic diabetes insipidus in some cases.

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