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Case Report

Traumatic brain injury inducing swift transition from syndrome of inappropriate antidiuretic hormone secretion to central diabetes insipidus: a case report

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Highlight

- This is a report of the patient who developed CDI on the day after a mild TBI and changed the endocrine condition to SIADH in a day.
- Changes from SIADH to CDI are commonly observed in patients with brain surgery or severe TBI, and their changes takes several days or weeks.
- The new points of this patient are that TBI was mild and that a change from SIADH to CDI occurred in a day.

Abstract. Heavy traumatic brain injury (TBI) may lead to the manifestation of either syndrome of inappropriate secretion of antidiuretic hormones (SIADH) or central diabetes insipidus (CDI). We present a case of TBI where SIADH transformed into CDI within a remarkably short timeframe. A previously healthy 4-yr-old boy was admitted to our hospital with hyponatremia and elevated urinary sodium level on the day following a traumatic head injury. Within 150 min after initiating SIADH treatment, a significant increase in urine volume and a decrease in urinary sodium levels were observed. Therefore, the treatment plan was modified to include desmopressin. By the 5th day of admission, the urine volume gradually stabilized and normalized without the need for further desmopressin treatment. Mild TBI can give rise to various conditions that may undergo rapid changes. Closely monitoring serum and urine electrolytes, along with urine volume, is imperative for the administration of appropriate and timely treatment.

Key words: traumatic brain injury, syndrome of inappropriate secretion of antidiuretic hormone, central diabetes insipidus

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Introduction

Traumatic brain injury (TBI) stands as a significant contributor to mortality and disability in children (1, 2). Various pathological conditions, such as cerebral salt wasting syndrome (CSWS), syndrome of inappropriate secretion of antidiuretic hormone (SIADH), and central diabetes insipidus (CDI), may manifest following TBI (2–6).

Hyponatremia emerges as the most prevalent electrolyte abnormality encountered in patients with TBI, with its incidence ranging from 9.6% to 51% (5). Following TBI, hypernatremia attributed to CDI is also observed, with an incidence reported between 2.6% and 51% (3). The disruption of sodium and water homeostasis poses a potential life-threatening situation, necessitating treatment tailored to the pathological conditions. Therefore, timely diagnosis and appropriate intervention are paramount in ensuring sodium homeostasis.

In this report, we present a case involving mild TBI wherein SIADH progressed to CDI. Patient sodium and water balance underwent rapid and dramatical changes, presenting a unique clinical course that yields valuable insights for the management of sodium and water balance following TBI.

Patient Description

A previously healthy 4-yr-old boy was referred and admitted to the Department of Pediatrics at Kagoshima City Hospital. Notably, his mother had undergone bone marrow transplantation for aplastic anemia when she was 4 yr old.

The day before admission, the patient fell off the second step on a concrete floor at his family home. Although he used both hands to support himself during the fall, he sustained a bruise on his head. Immediately after the incident, the patient was able to walk normally and did not experience a loss of consciousness. However, on the following day, he presented with two episodes of vomiting and convulsions, each lasting several minutes. Concerned about his decreased level of consciousness, the patient visited a local doctor and was subsequently referred to our hospital.

Upon admission, the patient weighed 14.0 kg (–1.2 standard deviation), with a blood pressure of 111/67 mmHg and a heart rate of 80/min. The level of consciousness, determined using the Glasgow Coma Scale, was E-1, V-1, M-1. A contusion wound of 1 cm length was observed on the left side of the head. Pupils were measured at 2 mm on both sides, with rapid contralateral reflexes. Deep tendon reflexes were within normal limits. Blood examination revealed marked hyponatremia (109 mmol/L) with no elevation in hematocrit or urea nitrogen levels (**Table 1**). Serum osmolality was low (227 mOsm/kgH_2O), urine osmolality was high (422 mOsm/kgH_2O), and the urinary sodium level was elevated (154 mmol/L). Endocrinological findings indicated that an arginine vasopressin value of 2.6 pg/mL, and thyroid and adrenal functions were within normal ranges (thyroid stimulating hormone, 1.07 μIU/mL; free triiodothyronine [T_3], 3.16 pg/mL; free thyroxine (T_4), 1.18 ng/dL; adrenocorticotropic hormone, 9.2 pg/mL; cortisol, 7.3 μg/dL; plasma renin activity (PRA), 0.3 ng/mL/h; aldosterone, < 17.0 pg/mL). Computed tomography (CT) of the head showed no abnormalities, including fractures or hemorrhages. Chest radiography revealed a cardiothoracic ratio (CTR) of 48%, with no abnormalities in the lung fields.

Table 1. Laboratory findings at admission

Hematology	
White blood cell counts	19,000 /μL
Red blood cell counts	408×10^4/μL
Hemoglobin	11.3 g/dL
Hematocrit	31.8%
Platelet counts	38.7×10^4/μL
Osmotic pressure	
Serum	227 mOsm/kgH_2O
Urine	422 mOsm/kgH_2O
Biochemistry	
Alanine aminotransferase	37 U/L
Lactate dehydrogenase	483 U/L
Total birilubin	0.8 mg/dL
Total protein	5.8 g/dL
Albumin	3.8 g/dL
Blood urea nitrogen	5.6 mg/dL
Creatinine	0.16 mg/dL
Sodium; serum	109 mmol/L
Urine	154 mmol/L

The patient was treated for hyponatremia with an infusion of 3% sodium chloride (NaCl) (3 mL/kg/h). Within 1 h, the serum sodium level increased to 118 mmol/L, exceeding the expected rise of 2.5 mmol/L/h (**Fig. 1**).

We switched to 0.9% NaCl infusion, but after 90 min, the serum sodium level increased to 120 mmol/L, accompanied by a sudden increase in urine volume to approximately 300 mL within 1 h. The infusion of 0.9% NaCl was transitioned to a 5% glucose solution. However, the serum sodium level continued to rise to 126 mM. Patient chest X-ray showed a reduced CTR from 48% at admission to 38%, and echocardiogram revealed a decrease in the left ventricular end-diastolic diameter from 32.9 mm (100% normal) (7) at admission to 29.9 mm (92% normal). Urinary sodium decreased to 18 mmol/L, and urine osmolality was 15 mOsm/kgH_2O. Simultaneously, the amount of supplemental fluid and hydration from the gastric tube increased with urine volume. Intranasal desmopressin at a dose of 3 to 4 μg per dose was administered the following day as patient urine volume further increased to 8,045 mL/d; thereafter, urine volume gradually stabilized, and serum sodium level normalized (**Fig. 2**). Desmopressin administration was discontinued on the 5th day after admission.

On the 4th day of admission, T1 weighted magnetic resonance imaging (MRI) of patient head revealed normal

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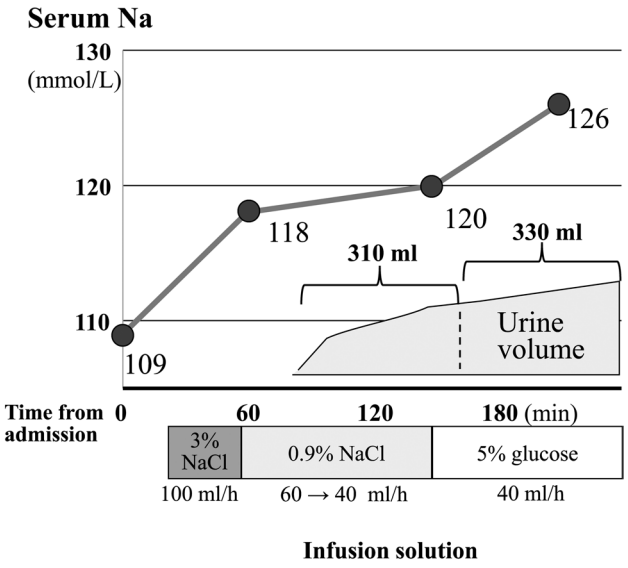

Fig. 1. Changes in serum sodium concentration after the initiation of treatment. Treatment commenced with a 3% sodium chloride solution infusion, resulting in a rise in patient sodium level to 118 mmol/L, surpassing the expected levels. The treatment was then shifted to a 0.9% sodium infusion. Subsequently, the urine volume notably increased, accompanied by a further rise in serum sodium level despite the administration of a 5% glucose solution.

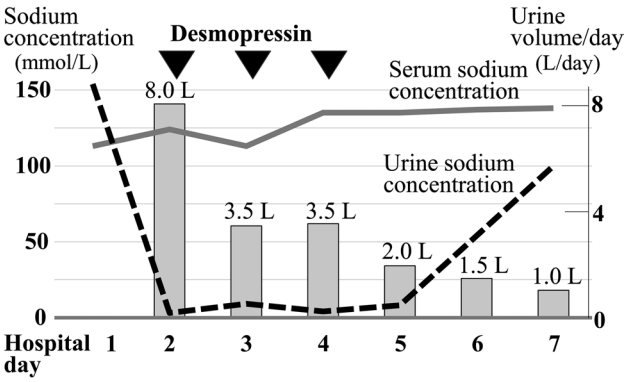

Fig. 2. Changes in serum and urine sodium concentration and daily urine volume. On the 2nd day of admission, the urine volume surged to 8.0 L, prompting the initiation of intranasal desmopressin administration. As the urine volume gradually decreased, desmopressin administration became unnecessary by the 5th day of admission. Concurrently, serum sodium concentration normalized gradually, and the initially elevated urine sodium concentration witnessed a substantial decrease dramatically after the urine volume increased. Patient urinary sodium level increased to 100 mmol/L.

findings, with no abnormalities. It also revealed a high signal intensity in the posterior pituitary gland (**Fig. 3**). No changes associated with head injuries were observed. The urine osmolality before desmopressin administration on the same day was 98 mOsm/kgH_2O, increasing to 368 mOsm/kgH_2O 90 min after administration.

On the 7th day of admission, patient serum sodium level was 139 mmol/L, urine volume was 1.0 L/day, urine osmolality was 385 mOsm/kgH_2O, and urine sodium level was 100 mmol/L.

Discussion and Conclusions

The patient was admitted to the hospital due to convulsions and a decreased level of consciousness resulting from hyponatremia. At the time of admission, the patient presented with hyponatremia, low serum osmolality, high urinary sodium levels, and high urine osmolality, necessitating differentiation between CSWS and SIADH (4–6). On admission, it was assumed to be SIADH because the patient did not experience any fluid loss, such as weight loss, tachycardia, or increased hematocrit. After initiating treatment with 3% NaCl for SIADH, his urine volume suddenly increased, accompanied by a decrease in urine osmolality and an increase in serum sodium levels. Desmopressin administration decreased urine volume and increased urine osmolality, confirming that his condition changed from SIADH to CDI.

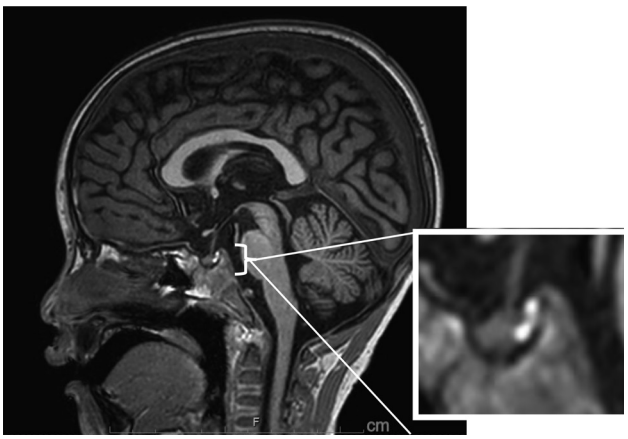

Fig. 3. Magnetic resonance imaging scan of patient head on the 4th day of admission. Magnetic resonance imaging on T1 weighted scan of the head revealed no alterations related to the head injury. A high signal intensity was observed in the posterior pituitary gland.

Following TBI, functional abnormalities associated with the direct impact, hypothalamic ischemia, or hemodynamic disturbances may lead to CSWS, SIADH, or CDI (2, 3). TBI may release presynthesized antidiuretic hormone (ADH), resulting in SIADH (2, 4). Hyponatremia due to SIADH leads to convulsions and decreased consciousness in the present case. After the release of ADH, hypothalamic ADH-producing neurons are disturbed and develop CDI after SIADH. The ADH synthesis disorder was temporary, and MRI on the 4th day of admission revealed a high signal in

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the posterior pituitary gland, indicating that ADH had already been produced at that time (8). Therefore, nasal administration of desmopressin was no longer necessary on the day of admission.

Surgery of the sellar region is often accompanied by postoperative disturbances in sodium and water homeostasis. Several patients (4.5%–15.7% of transsphenoidal pituitary adenoma surgeries) show a triphasic response, which is characterized by CDI immediately after the operation, followed by hyponatremia a few days later and permanent CDI starting approximately 1 week after the operation (9, 10). The mechanism of the triphasic response is thought to be as follows: the initial phase of CDI occurs due to the stunning of ADH neurons and the inability of the posterior pituitary to secrete ADH; the second phase of SIADH results from the unregulated release of ADH; and the third phase of permanent CDI is due to the absence of ADH in the posterior pituitary gland and no ADH production (10, 11).

Goel *et al*. reported the case of a 20-yr-old man who exhibited a triphasic response after TBI (11). He was admitted to the hospital 5 d following TBI, presenting with subarachnoid hemorrhage, subdural hematoma, and bone skull fractures. CDI developed on the 2nd day of hospitalization (6 d after TBI), followed by SIADH on the 7th day in the hospital, and permanent CDI starting on the 11th day in the hospital.

Compared with patients with a triphasic response, the patient in this case demonstrated a biphasic response, lacking the first phase of CDI. In the third phase, the CDI was temporary. The damage from TBI was considered mild, as no intracranial hemorrhage or bone fractures were observed. This mild damage likely contributed to these differences; the damage was so mild that the stunning of ADH neurons in the initial phase and permanent disturbance of ADH productivity in the third phase did not occur. Importantly, these ADH abnormalities can occur even with mild damage, as similar cases have been previously reported (12–14). Another specific and crucial point was the rapid and dramatic change in his sodium and water balance over a very short period. The patient was admitted and developed CDI following SIADH on the day after TBI, whereas patients with a triphasic response start the third phase of DI ≥ 1 wk after the operation or TBI.

Pediatric brain injury exhibits unique biomechanical properties due to a combination of higher plasticity and deformity, resulting in the absorption of external forces in a manner distinct from adults (15). The heightened plasticity of the skull in children results in shared forces between the skull, adjacent cortical vessels, and the brain. These shared forces may result in the stretching and sharing of injuries to the brain parenchyma (15). Such injuries to the pituitary gland and hypothalamus, involving stretching and sharing, may contribute to the observed SIADH and CDI in this case.

In a study by Inoue *et al*. (16), 13 patients developed CDI after head injuries. Among them, five patients who developed CDI within 12 h of injury (early group) showed diffuse axial damage in addition to damage in the hypothalamic region, unlike the remaining eight patients who developed CDI 12 h after injury (delayed group). The high signal in the posterior pituitary gland disappeared and reappeared over time in the delayed group but did not reappear in the early group. In this case, the course was aligns with that of the delayed group, except that the patient presented with low serum sodium levels due to SIADH immediately before the onset of CDI.

The treatment of SIADH is markedly different from that of CDI. SIADH is typically managed through fluid restriction and correction of hyponatremia via high-concentration sodium infusion (4, 6), whereas CDI treatment involves free water supplementation with a 5% glucose solution and desmopressin administration (2, 6). Therefore, carefully evaluating patient condition and applying appropriate treatment is crucial. In our case, we had to make swift decisions, transitioning our treatment strategy from infusing a high-concentration sodium solution with restricted volume to a low-concentration sodium solution with a higher volume. Rigorous monitoring of the patient, including vital signs, serum and urine electrolytes, and urine volume, was maintained on an hourly basis until his condition stabilized. This vigilant observation enabled us to promptly identify any sudden changes in patient condition and administer the necessary treatment.

In this report, we present a unique case of TBI wherein patient condition transitioned swiftly from SIADH to CDI. Given the potential for diverse conditions and rapid changes following TBI, close monitoring of serum and urinary sodium levels, urine volume, and osmolality is essential, enabling the administration of timely and appropriate treatment.

Conflict of interests: The authors have nothing to declare.

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