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Case Report

Development of Inappropriate Vasopressin Secretion in Association With Lumbar Cerebrospinal Fluid Drainage in an Adult With Traumatic Basilar Skull Fracture

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ABSTRACT

Objective: Hyponatremia associated with cerebrospinal fluid (CSF) drainage is primarily limited to pediatric patients. Only 1 case in an adult, after pituitary surgery, has been described. We present the first adult case, to our knowledge, of lumbar CSF drainage associated with the syndrome of inappropriate antidiuretic hormone (SIADH) in a patient with a traumatic basilar skull fracture.

Methods: Serum and urine samples were evaluated for hyponatremia. Computed tomography and magnetic resonance imaging were performed to evaluate the fractures.

Results: A 31-year-old woman was hospitalized with traumatic facial and skull base fractures and managed conservatively. Four days into her hospital stay, she underwent lumbar CSF drainage for 6 days to treat a CSF leak. On examination, the patient remained hemodynamically stable and euolemic. Sodium levels decreased from 142 to 136 mmol/L (normal, 135–146 mmol/L) on the day before and after lumbar drain placement, respectively, down to a nadir of 124 mmol/L over 3 subsequent days. Serum osmolality was 260 mOsm/kg (275–295 mOsm/kg); urine osmolality, 482 mOsm/kg; urine Na, 175 mmol/L; and thyroid-stimulating hormone, 4.0 μ IU/mL (0.3–4.7 μ IU/mL). The patient received treatment with sodium tablets, fluid restriction, and hypertonic saline for a diagnosis of SIADH. Sodium levels normalized from 131 to 136 mmol/L within 16 hours after lumbar drain removal.

Conclusion: This case illustrated a temporal association of SIADH with CSF drainage in an adult. Although this could be coincidental because a basilar skull fracture can lead to SIADH, it raises the possibility that CSF lumbar drainage contributed to the patient's SIADH.

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Introduction

We present the first case, to our knowledge, of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) associated with lumbar cerebrospinal fluid (CSF) drainage for the treatment of CSF leak in a previously healthy young adult patient following a traumatic skull fracture. The only other reported case in an adult occurred following pituitary surgery.¹ Cases of hyponatremia due to CSF drainage reported in the literature otherwise appear limited to

the pediatric population, where the direct loss of sodium content with CSF drainage leads to hyponatremia.^{2–4}

Case Report

A 31-year-old woman presented with critical trauma after a fall off a bicycle at a speed of 25 miles per hour. She sustained a right epidural hematoma and multiple facial fractures as confirmed on computed tomography and magnetic resonance imaging, including the bilateral temporal bones, right orbital bone, right zygomatic arch, and sphenoid skull base, complicated by a CSF leak. After extubation and negative continuous electroencephalogram monitoring, the patient was downgraded to the regular neurosurgery ward. Her fractures and CSF leak were conservatively managed.

The patient's laboratory findings were initially unremarkable during her hospitalization, other than mild anemia with a hemoglobin level of 10.4 g/dL (normal, 13.7–17.5 g/dL), with normal

Abbreviations: AVP, arginine vasopressin; CSF, cerebrospinal fluid; SIADH, syndrome of inappropriate antidiuretic hormone.

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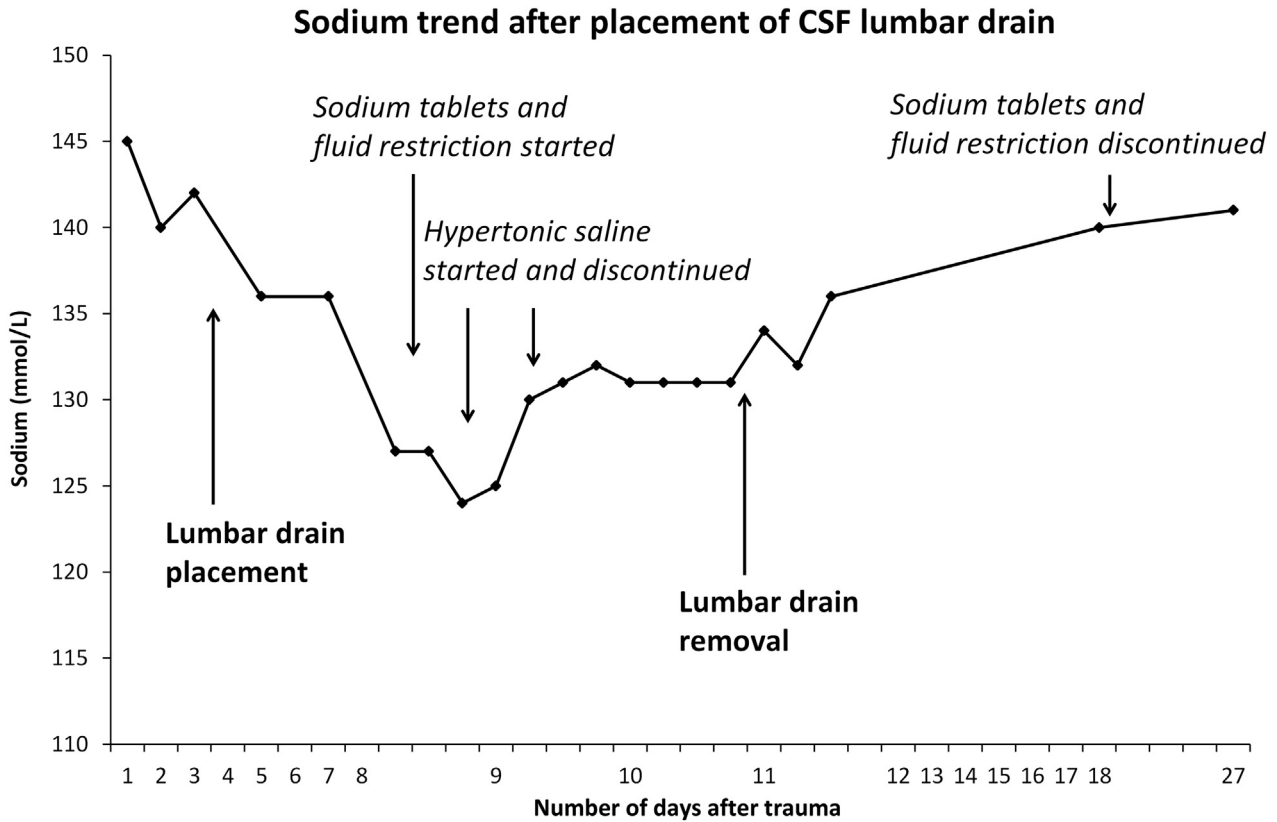


Fig. 1. Serum sodium trend after the patient’s critical trauma (day 1). Following the placement of a lumbar CSF drain, the patient developed hyponatremia, with laboratory test results consistent with the syndrome of inappropriate antidiuretic hormone secretion. The patient’s hyponatremia was resistant to treatment with sodium tablets and fluid restriction, and after reaching a sodium nadir of 124 mmol/L (135–146 mmol/L), hypertonic saline was started. After discontinuation of hypertonic saline, mild hyponatremia persisted, with sodium levels in the low 130s (in mmol/L) until removal of the lumbar CSF drain. The sodium levels normalized within less than 16 hours of the drain removal. CSF = cerebrospinal fluid.

kidney function and sodium levels ranging from 142 to 145 mmol/L (normal, 135–146 mmol/L) for the first 3 days of the hospital stay. Owing to the continuing CSF leak, confirmed with beta-2 transferrin testing, a lumbar drain was placed 4 days into the hospital stay, draining at 10 mL/hour. The sodium levels subsequently dropped from 142 to 136 mmol/L from the day before and after lumbar drain placement, respectively, down to a nadir of 124 mmol/L over the following 3 days. The sodium levels continued to decrease while on a maintenance normal saline infusion at 100 mL/hour. Hypovolemia and cerebral salt wasting as potential causes of hyponatremia were, thus, thought to be unlikely.

The patient’s clinical picture, other than the lumbar drain placement, remained stable, and she denied symptomatic changes. Nausea and pain, which are potent stimulators of arginine vasopressin (AVP),⁵ were mild and well controlled. The patient was hemodynamically stable and euvoletic. There were no clinical signs and symptoms of adrenal insufficiency, and thyroid-stimulating hormone levels were normal at 4.0 µU/mL (0.3–4.7 µU/mL). Laboratory testing showed serum osmolality at 260 mOsm/kg (275–295 mOsm/kg), urine osmolality at 482 mOsm/kg, urine Na at 175 mmol/L, and urine creatinine at 43.7 mg/dL, albeit collected after being on normal saline infusion and the initiation of salt tablets.

The patient was treated for a diagnosis of SIADH, and sodium trends in relation to the lumbar drain placement and treatment were carefully monitored (Fig. 1). The patient was initially placed on a trial of salt and fluid restriction, with a continued decrease in sodium levels. She was then treated with hypertonic saline 4 days

after the lumbar drain placement, increasing the sodium level from a nadir of 124 to 130 mmol/L. After discontinuation of hypertonic saline, the patient’s sodium stabilized at 131 to 132 mmol/L for 2 days on salt tablets (1 g 3 times daily) and a fluid restriction of 1 L. The lumbar drain was removed 6 days after placement, with normalization of sodium values from 131 to 136 mmol/L within less than 16 hours. The patient’s sodium levels remained normal after discontinuation of sodium tablets and fluid restriction.

Discussion

The case is the first, to our knowledge, of SIADH associated with lumbar CSF drainage in an adult with a traumatic basilar skull fracture, when the development and resolution of hyponatremia were tightly correlated with the placement and removal of the lumbar drain. Notably, the patient’s lumbar drain removed CSF at 10 mL/hour for 6 days, during which time the patient’s sodium level dropped, reaching a nadir at 124 mmol/L. The patient’s hyponatremia was refractory to treatment with fluid restriction and sodium tablets, and treatment with hypertonic saline was initiated. The patient continued to be hyponatremic, even with treatment, until lumbar drain removal.

Based on our literature review, the other adult patient with SIADH associated with lumbar CSF drainage was a 53-year-old acromegalic patient. This patient developed hyponatremia down to a nadir sodium level of 110 mmol/L 6 days after transsphenoidal surgery for a 0.5 × 0.5-cm adenoma.¹ The CSF was drained at 10 to 15 mL/hour over 5 days, with a total of 1350 mL drained. Euvolemia

was confirmed with central venous pressure readings. This patient also did not respond to fluid restriction and was treated with hypertonic saline.

The remaining cases of hyponatremia in the setting of CSF drainage are limited to pediatric cases. In infants, CSF drainage via repeated lumbar punctures, ventricular taps, externalized ventricular drains, ventriculoperitoneal shunts, and even CSF leak has been associated with hyponatremia due to direct sodium losses in the CSF.^{2–4} The sodium concentration of CSF ranges from 135 to 150 mmol/L.⁴ Sodium loss in a typical ventricular tap of 20 mL can be as much as 3 mmol,² whereas the daily sodium intake of a term infant would be around 6 mmol.⁴ These infants are treated with oral sodium supplementation.^{2–4} Though hyponatremia with CSF drainage in pediatric patients is causal, direct sodium loss from CSF drainage would not explain hyponatremia in adults.

In these 2 adult cases, the temporal association of hyponatremia with CSF drainage brings up the possibility that continuous lumbar CSF drainage, over the course of 5 to 6 days for these patients, exacerbated their underlying significant risk factors for SIADH. Transphenoidal surgery can lead to a triphasic pattern of post-operative water balance.⁶ Following the initial phase of diabetes insipidus in the first 24 to 48 hours after surgery, SIADH may occur 5 to 8 days after surgery and last 2 to 5 days.⁶ Permanent diabetes insipidus can occur in the third phase if more than 85% to 90% of the hypothalamic magnocellular neurons are damaged.⁶ Traumatic brain injury, particularly basilar skull fractures, can similarly lead to anterior and posterior pituitary dysfunction.⁷

Both patients' hyponatremia developed at the expected timing of an isolated SIADH phase of the triphasic response following pituitary trauma. It is thus possible that the timing of hyponatremia development with lumbar CSF drainage was coincidental. However, the degree of hyponatremia in the patients, refractoriness to fluid restriction, and treatment with hypertonic saline raise the question of whether extended CSF drainage contributed to a more severe SIADH in these patients.

Both the patients' clinical pictures were consistent with SIADH. SIADH has 4 subtypes.⁸ Type A involves supraphysiologic, random secretion of AVP, often from malignancies. Type B is due to reset osmostat, leading to AVP secretion at lower plasma osmolalities than normal, though the pathophysiologic mechanism is unknown. Types C and D are rare, with type C involving persistent low-grade basal AVP secretion due to possible dysfunction of inhibitory neurons in the hypothalamus. Type D is due to nephrogenic SIADH, including a rare gain-of-function mutation in vasopressin receptor 2, despite undetectable AVP secretion.

We query whether continuous lumbar CSF drainage in the adult patients affected the local CSF milieu and led to reset osmostat, resulting in SIADH. AVP is classically thought to be controlled by osmoreceptors in the hypothalamus that detect plasma osmolality and peripheral baroreceptors that provide feedback on volume status.⁹ However, studies suggest the presence of intracranial baroreceptors as well.^{10,11} A study in rats showed that infusion of artificial CSF into the cerebral ventricle, effectively the opposite of CSF drainage, led to significant decreases in plasma AVP levels compared with those in controls.¹⁰ By contrast, lumbar CSF drainage is designed to treat conditions such as CSF leak with a negative pressure gradient; overdrainage rarely leads to intracranial hypotension.¹² We hypothesize that lumbar CSF drainage, especially with longer durations, as in our patients, may increase AVP release by decreasing central CSF pressure and lead to reset osmostat.

Though lumbar CSF drainage is a common procedure, hyponatremia has rarely been reported in adults. These 2 adult patients were unusual in that they both had underlying risk factors for SIADH and underwent a longer duration of CSF lumbar drainage for 5 to 6 days. We query if extended CSF drainage compounded their underlying risk of SIADH, leading to more severe hyponatremia. It is also notable that only a few reports have investigated the use and complications of continuous lumbar CSF drainage,¹³ bringing up the possibility of under-reporting of hyponatremia as well.

Conclusion

The association of CSF drainage with hyponatremia in adults has been rarely reported, though well described in the pediatric literature. We present the first case, to our knowledge, of SIADH associated with lumbar CSF drainage in an adult patient with a traumatic basilar skull fracture, which can be associated with a pituitary injury. The other adult case occurred in an acromegalic patient following pituitary surgery. The timing of the patients' hyponatremia correlated not only with lumbar CSF drainage but also with the SIADH phase of the triphasic response. Both patients underwent CSF drainage for a longer duration, over the course of 5 to 6 days, and were treated with hypertonic saline. We hypothesize that extended CSF drainage contributed to a more severe picture of SIADH in these patients who had underlying risk factors for the development of reset osmostat.

Disclosure

The authors have no multiplicity of interest to disclose.

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