Hydrophobia Associated with Severe Hypernatremia, Acute Kidney Injury, and Rhabdomyolysis

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Case

A 33-year-old male was brought to the emergency department (ED) by his family with a 10-day history of decreased to no oral intake and a progressive unsteady gait. He had a known history of major depressive disorder, agoraphobia, acrophobia, and hydrophobia, which had not been treated with any medications; he had been followed up by outpatient psychiatry.

On arrival at the ED, he was noted to be drowsy, with a Glasgow Coma Score (GCS) of 14/15 (E4, V4, M6), blood pressure of 85/40 mm Hg, heart rate of 140 beats/minute, temperature of 38.5ºC, respiratory rate of 38 breaths/minute, and oxygen saturation at 95% on room air. He was noted to be severely dehydrated with dry mucous membranes, a flat jugular venous pressure, mottled skin, and anuria. He was resuscitated in the ED with 4 L of intravenous normal saline over 4 hours and started on empiric intravenous antibiotics, piperacillin-tazobactam 4.5 g IV q6h, for presumptive septic shock.

The initial laboratory examination revealed the following: a serum sodium level of 210 mmol/L, potassium level of 5 mmol/L, chloride level of 165 mmol/L, bicarbonate level of 22 mmol/L, blood urea nitrogen (BUN) at 37.1 mmol/L, serum creatinine at 922 µmol/L, serum osmolality at 459 mOsm/L, creatinine kinase (CK) at 13,600 U/L, white blood cell count of 18 × 10⁹/L, hemoglobin level of 20 g/L, platelets at 85 × 10⁹/L, hematocrit of 0.61, lactate at 8.7 mmol/L, aspartate transaminase (AST) level of 536 U/L, lipase level of 264 U/L, serum amylase level of 248 U/L, serum albumin at 57 g/L, and total bilirubin at 20 µmol/L. The screenings for toxic drugs and substances upon admission were negative, and the initial chest radiograph and computed tomography (CT) of the head were normal. The patient was transferred to the intensive care unit (ICU) for continuing fluid resuscitation and hemodynamic monitoring. After the initial normal saline bolus, infusions at 200 cc/h were performed to treat the ongoing dehydration and severe hypernatremia. His serum sodium was monitored closely every 2 hours; the goal was to lower it by 10–15 mmol/L over 24 hours (Figure 1).

At 24 hours’ post-admission, our patient’s serum sodium levelled to 191 mmol/L. The intravenous fluid was switched to half normal saline at 200 cc/h, coupled with an infusion of free water through a nasogastric tube at a rate of 120 cc/h. At 48 hours’ post-admission, his serum sodium had improved to 169 mmol/L (Figure 2). On day 3 of his admission, it was noted that his serum creatinine and CK continued to climb, reaching 1,136 µmol/L and >22,500 U/L, respectively (Figure 3 and 4). He continued to be anuric, with a total cumulative fluid balance of >12 L since admission. Hemodialysis (HD) was initiated for worsening of acute kidney injury and CK level; he was also intubated for mechanical ventilation to protect his airway from increasing somnolence due to worsening uremia (Figure 5).

A repeat CT of the head did not reveal any abnormality. A sub-hairline electroencephalogram was also performed, and it did not reveal any seizure activities. Our patient received HD...
daily for 3 days; he was then switched to continuous veno-
venous hemodialysis (CVVHD) due to persistent hypotension
secondary to presumptive worsening sepsis. His initial blood
culture in the ED was negative, but the sputum culture was
positive for Enterobacter aerogenes, which was resistant to
piperacillin-tazobactam; subsequently, his antibiotics were
changed to imipenem 500 mg IV q6h. He was switched back to
intermittent hemodialysis on day 7 of his admission to the ICU
when he became hemodynamically stable. His serum sodium,
CK, and neurological status continued to improve, and he was
extubated on day 15 of admission to the ICU. He was
discharged home under his family’s care after a 1-month
hospital stay.

Discussion
Hypernatremia is a relatively uncommon cause of ICU
admission, and includes only 2% of the admitted patients. This
is because thirst, one of the most powerful human behavioural
drives, which is regulated by serum osmolality through the
control feedback loop of antidiuretic hormone (ADH), spurs a
person to seek out and drink water. When thirst is maximally
stimulated in human beings, the craving for water cannot be
ignored, and it can become sufficiently intense to dominate all
other thoughts and sensations.

There are only four reported cases of a psychiatric patient
presenting with hypernatremia, and none of the cases
required ICU admission and renal replacement therapy. Here
we report the first case of severe hypernatremia due to
hydrophobia that required ICU admission and that was
complicated by rhabdomyolysis and acute kidney injury.

Hypernatremia can result from administration of
hypertonic sodium solutions, but it occurs more commonly
due to a loss of free water in patients such as sick infants, the
elderly, and adults with limited access to water, impaired mental
status, or an abnormal thirst drive. Thirst is one of the most
powerful behavioural drives that can be experienced by human
beings. The threshold for thirst sensation varies widely among
healthy individuals, but it usually occurs at a serum plasma
osmolality of approximately 290 mOsm/kg. Above this
threshold, the thirst sensation increases rapidly, and it becomes
significantly intensified at serum plasma osmolalities of
300–305 mOsm/kg. To overcome this strong thirst drive
sensation sufficiently to result in a severe metabolic
abnormality such as hypernatremia, a significant anatomical or
psychogenic disturbance is required. This is usually seen in
adults who have a pathological process involving the
destruction of the hypothalamus or supraoptico-hypophyseal
system. But psychogenic oligodipsia is not only an extremely
rare condition, it is an even less common presentation of the
hyperosmolar syndrome, which can often go unrecognized in some psychiatric patients.\(^1\) Psychogenic polydipsia with hypernatremia is a well-documented condition in psychiatric patients,\(^7,8\) but there are only four reported cases of psychogenic adipsia leading to hypernatremia requiring medical management.\(^1\) None of reported cases was complicated by rhabdomyolysis and acute kidney injury requiring renal replacement therapy.

Rhabdomyolysis due to hypernatremia and hyperosmolality is a rare complication,\(^9\) and its mechanism is unknown. Grinstein et al.\(^{10}\) suggested that during the shrinkage of the cells in the hypertonic medium, the normal cell volume is kept by means of an Na\(^+\)/H\(^+\) antiport and Cl\(^-\)/HCO\(_3^-\) exchange at the level of the cell membrane. However, in many cell types, the activation of the antiport is also mediated by an increase in intracellular calcium. After a significant serum hypertonic stress, the intracellular calcium will reach a maximum level in 6–8 minutes and give rise to the activation of protein kinases and result in cell lysis. Due to this cell lysis, muscle enzymes are liberated and rhabdomyolysis develops. Evidence for a direct causal link between hypernatremia and rhabdomyolysis is provided by three reported cases of central diabetes insipidus resulting in severe hypernatremia and rhabdomyolysis in the absence of other potential causes.\(^{11–13}\) In all cases, the serum sodium concentration was >180 mmol/L. Abramovici and colleagues, reporting a case series of 18 patients with hypernatremia, showed a significant linear correlation between serum sodium concentration and serum CK level.\(^9\)

**Conclusion**

Our patient suffered from a psychiatric illness involving severe water phobia that interfered with his thirst drive and led to severe hypernatremia. This resulted in a worsening neurological status followed by rhabdomyolysis and acute kidney injury, which required ICU admission and renal replacement therapy. This case provides evidence that hypodipsia or adipsia from psychiatric disturbances causing severe hypernatremia can occur and is potentially reversible.

**References**