CLINICAL VIGNETTE

An Unquenchable Thirst: A Case of Water Intoxication

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A 26-year-old physically active woman with no significant medical problems presented to the emergency department with acute onset of confusion and disorientation. Three weeks prior to presentation, her primary care provider evaluated her for episodes of dizziness and tunnel vision that she developed after strenuous exercise. These symptoms were attributed to dehydration, and she was advised to hydrate aggressively after activity. On the day of presentation, she completed a five-mile run. She drank 3-4 liters of water to maintain adequate hydration. Shortly after, she developed a feeling of euphoria, dizziness, and paresthesia's in her upper extremities. Her mother brought her to the Emergency Department (ED) after discerning irrational thought processes. In the ED, her blood pressure was 109/78 mmHg with a heart rate of 96, respiratory rate of 14, and afebrile temperature, with 99% oxygenation saturation on room air. She appeared in no acute distress, and was alert with fluent speech and intact memory. Her mucous membranes were moist and there was no meningismus, jugular venous distension or thyromegaly. A detailed cardiovascular, pulmonary, abdominal, and neurologic examination was otherwise unremarkable. Her past medical, surgical, and family history were only notable for episodic use of Valacyclovir 1000 mg for genital and oral herpes simplex virus (HSV) infection flares.

Initial laboratory evaluation was pertinent for a sodium of 129 mEq/L, potassium of 3.3 mEq/L, blood urea nitrogen of 7 mg/dL and creatinine of 0.7 mg/dL. Her urinalysis revealed a specific gravity of less than 1.005, while serum osmolality was 262 mOsm/kg, urine osmolality was 81 mOsm/kg, urine sodium was 31mmol/L, and urine creatinine was less than 5 mg/dL. Her complete blood count (CBC), liver laboratory tests, TSH, and cranial computed tomography (CT) images were unremarkable. She received one liter of normal saline in the ED and was admitted to the telemetry unit for further management. A repeat sodium level drawn four hours after admission was 139 mEq/L, with urine output of 1.5 liters in the first two hours. Given concern for overly rapid correction of her serum sodium and subsequent potential neurologic sequelae, she was started on 5% dextrose intravenously with free water at a rate of 6mL/kg for two hours. A repeat sodium level remained 139 mEq/L. She was given 2 mcg of intravenous desmopressin, and fluid restriction of 1.5 liters per 24 hours was initiated. After stabilization of her sodium level in the 132 mEq/L range, she was asymptomatic without neurologic deficits, and was discharged 12 hours later with instructions to minimize fluid intake especially with activity.

Discussion

Hyponatremia is commonly defined as a serum sodium concentration below 135 mEq/L. It can result from excess water intake or low water excretion that is low, or a combination of these abnormalities. Causes of hyponatremia are classified according to the body's ability to excrete dilute urine and if impaired, the reason for the impairment. Hypotonic hyponatremia is the most common form of hyponatremia in clinical practice. Hypotonic hyponatremia results from the intake and subsequent retention of water.[1] The typical physiologic response to hyponatremia involves excretion of large volumes of free water in the urine with low sodium and potassium concentration. When water is ingested or absorbed causing even slight hypotonicity, both thirst and antidiuretic hormone (ADH) release are normally suppressed.[2] ADH is produced by hypothalamic neurons that receive inputs from osmoreceptors that respond to the serum sodium concentration and from baroreceptors that respond to the status of the circulation.[3] Suppression of ADH secretion requires normal functioning of osmoreceptors and the absence of signals from baroreceptors that can stimulate ADH release even when the serum sodium concentration is low. Excretion of electrolyte-poor water is accomplished by reabsorbing salt without water in the water-impermeable ascending limb of the loop of Henle and distal convoluted tubule. Excretion of electrolyte-poor water also requires that the later distal tubule segments and collecting duct are relatively impermeable to water. High levels of ADH result in insertion of water channels in the collecting duct while low levels of ADH allow these water channels to be removed from the epithelium.[4] In normal individuals a water load will be rapidly excreted as the dilutional fall in serum tonicity suppresses the release of ADH, thereby allowing excretion of the excess water as dilute urine. The normal diluting mechanisms of the kidney can produce urine with an osmolality as low as 50 mOsmol/kg. A typical western diet generates approximately 900 mOsmol of solute daily, which is composed of approximately one-half urea (derived from dietary protein) and one-half sodium and potassium salts. If the diet is lower in salt, potassium, and protein, the capacity to excrete large volumes of urine will be less. As an example, excretion of 200 mOsmol of solute at a concentration of 50 mOsmol/L will result in only 4 L of electrolyte-poor urine. This still provides an enormous range of protection against the development of hyponatremia since the daily fluid intake in

most healthy individuals is approximately 2 to 2.5 L/day. Patients with primary polydipsia can become hyponatremic as they overwhelm the excretory capacity of the kidney despite appropriate ADH suppression. Hyponatremia in primary polydipsia is usually mild since the excess water is readily excreted. However, water intake may occasionally exceed 400 to 600 mL per hour, which may produce fatal hyponatremia even though the urine is maximally dilute with an osmolality below 100 mOsmol/kg. Symptomatic hyponatremia can also be induced with an acute 3- to 4-liter water load.

The 2015 Third International Exercise-Associated Hyponatremia Consensus Development Conference defined exercise-associated hyponatremia (EAH) as hyponatremia occurring during or up to 24 hours after prolonged physical activity. A number of risk factors have been linked with the development of EAH.[3] The most important of these is sustained high fluid intake. In athletes who develop EAH, the excessive fluid intake reflects conditioned behavior based upon recommendations to drink fluid during exercise to avoid dehydration. Increased fluid intake is necessary but is not the sole explanation for many if not most cases of EAH.[4] The other major factor is impaired urinary water excretion due to persistent secretion of antidiuretic hormone (ADH) from intense exercise itself, nausea, vomiting, hypoglycemia, nonspecific stresses such as pain and emotion, and the release of muscle-derived interleukin-6. Other proposed mechanisms of hyponatremia include a failure to mobilize exchangeable sodium stores and sodium losses in sweat.[4] The goal of treatment for hyponatremia is to increase the serum sodium concentration by 4-6 mEq/L over the first 24 hours.[5] Correction of hyponatremia should never exceed 10 mEq/L over 24 hours as it carries the risk of Osmotic Demyelination Syndrome (ODS). The rate of correction is particularly important in the setting of chronic hyponatremia, when physiologic adaptation in the brain has already occurred. Patients with severe hyponatremia, chronic hyponatremia (duration of greater than 48 hours), hypokalemia, malnutrition, and liver disease are at increased risk of developing ODS. Symptoms usually manifest two to six days after the insult and may include speech and swallowing difficulty, weakness or paralysis, cognitive deficit, and coma. ODS is usually irreversible so it is imperative that rapid correction of hyponatremia is avoided if possible and treated carefully if it occurs.

A re-lowering of serum sodium can reverse the breakdown of the blood brain barrier that occurs with overly rapid correction and can prevent the infiltration of microglia that is a feature of osmotic demyelination.[6] The two most common regimens include dextrose 5%, 6 mL/kg of lean body weight, infused over two hours. The goal is to lower the serum sodium by approximately 2 mEq/L. The second regimen involves desmopressin 2 mcg intravenously or subcutaneously every six hours to decrease the exaggerated water loss through urine.

Our patient's low serum osmolality was consistent with hypotonic hyponatremia. The history of large volume free water intake prior to presentation, laboratory findings of low urine osmolality indicating maximal dilution of her urine by her renal tubules, and excretion of a noticeably large amount of urine in the first two hours after admission suggested that her hyponatremia was exercise induced hyponatremia from water intoxication. Her serum sodium rose from 129 mEq/L to 139 mEq/L within four hours of admission after providing solute-rich (0.9% normal saline) fluid, leading to concern for development of Osmotic Demyelination Syndrome. She was treated with 5% Dextrose infusion at the appropriate rate, but with inadequate response, and consequently required intravenous desmopressin. Two days after discharge, her sodium had normalized at 141 mEq/liter, with no further recurrent episodes of confusion, dizziness or paresthesias.

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