Severe hypernatraemia (221 mEq/l), rhabdomyolysis and acute renal failure after cerebral aneurysm surgery

Emerson Q. Lima, Filipe C. Aguiar, Daniela M. Barbosa and Emmanuel A. Burdmann

Nephrology Division, São José do Rio Preto Medical School, São José do Rio Preto, São Paulo, Brazil

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Introduction

Hypernatraemia is a relatively frequent electrolyte abnormality in hospitalized patients, with reported incidences ranging from 0.65 to 2.23% [1]. Normally, when the serum sodium rises, thirst develops and antidiuretic hormone (ADH) is secreted. Hypernatraemia will not occur in individuals with an intact thirst mechanism and free access to water, due to a potent osmolar stimulus to drink. Hypothalamic injuries may impair the function of the thirst regulatory centre, causing hypodipsia and hypernatraemia [2,3].

Severe hypernatraemia is a serious condition with a mortality of ≥60% [1,4]. We describe a case of a patient surviving extremely severe hypernatraemia (221 mEq/l sodium), rhabdomyolysis and acute renal failure (ARF) associated with hypodipsia and partial central diabetes insipidus after surgery to repair an aneurysm of the anterior communicating artery. Such severe hypernatraemia is unusual and there are few reported cases with serum sodium >200 mEq/l [5–8].

Case

A 53-year-old male was submitted to surgery (clipping) to repair an aneurysm of the anterior communicating artery. The post-operative period was uneventful and 7 days after the surgery he was discharged with serum creatinine of 1.0 mg/dl and serum sodium of 137 mEq/l. Following discharge the patient had episodes of confusion, despite being otherwise active and taking fluids appropriately. Approximately 17 days after the surgery, a decrease of the patient’s water intake was observed, he started to fall without reason and he presented with dysarthria, increasing irritability and somnolence. Twenty-five days after the surgery, he was brought to the emergency room (ER) of our hospital. At admission he was lethargic and clinically dehydrated. Glasgow coma scale was nine. Pupils were symmetric and reactive, axillary temperature was 36.4°C, blood pressure was 120/90 mmHg and heart rate was 110 beats/min. Initial laboratory evaluation (Table 1) showed haemoglobin 15.7 g/dl, haematocrit 48%, normal serum glucose, creatinine 5.4 mg/dl and serum sodium 221 mEq/l (confirmed). Urinalysis showed pH 5.0, specific gravity 1.026, 1+ protein, white blood cells (WBCs) 10 000/ml (normal range: < 10 000/ml) and red blood cells (RBCs) 2000/ml (normal range: < 10 000/ml). Spinal fluid was mildly haemorrhagic, with 69 RBCs/mm³, 8 WBCs/mm³, protein 112 mg/dl, glucose 62 mg/dl, absence of bacteria and negative culture. A computerized axial tomography (CAT) brain scan was normal, except for the presence of metallic clips.

The patient was transferred to an intensive care unit and was administered 0.45% NaCl intravenously (i.v.) with the addition of water and diet via a nasoenteric tube. On hospital day 2, increased serum creatine phosphokinase (CPK) was observed (Table 1). On the third hospital day, serum sodium was 179 mEq/l, urinary volume was 3.45 l/day and the patient had received 11.3 l of 0.45% saline i.v. plus 2.5 l water by nasoenteric tube. On hospital day 7, a nephrology consultation was requested due to maintained high serum creatinine. The patient had developed pneumonia, was on mechanical ventilation and was receiving ceftriaxone and metronidazole, with haemoglobin 9.4 g/dl, haematocrit 28%, sodium 148 mEq/l and creatinine 5.0 mg/dl. Laboratory evaluation was consistent with rhabdomyolysis: increased CPK, phosphorus and uric acid and decreased calcium and albumin. Hydration was maintained with i.v. 5% dextrose (3–4 l/day) and sodium bicarbonate was given to minimize deleterious effects of myoglobinuria. There was a progressive renal function improvement
serum creatinine 0.9 mg/dl on hospital day 19), normalization of serum sodium and resolution of pneumonia. On hospital day 38, the patient was discharged.

After 15 days he was re-admitted, was confused and presented serum sodium of 180 mEq/l and serum creatinine of 4.3 mg/dl. Serum osmolality was 381 mOsm/kg while urine osmolality was 492 mOsm/kg. Serum sodium and creatinine returned to normal after adequate hydration and the patient was discharged again.

He returned for follow-up 1 month later, had no complaints and laboratory results showed sodium 164 mEq/l, creatinine 2.0 mg/dl, serum osmolality 344 mOsm/kg and urine osmolality 608 mOsm/kg (after 6h of fasting). He was admitted to the nephrology ward for evaluation. During hospitalization it became clear that the patient had absence of thirst and did not drink water adequately, despite hypernatraemia, and a diagnosis of hypodipsia was established. After hydration and normalization of serum sodium and renal function, the patient’s response to ADH was evaluated. The administration of intranasal desmopressin (0.1 μg) raised urine osmolality from 290 to 443 mOsm/kg (serum osmolality changed from 310 to 304 mOsm/kg). A serum ADH level of 2.8 pg/ml (radioimmunoassay; normal range: < 8.0 pg/ml) was measured when serum sodium was 153 mEq/l, serum osmolality was 352 mOsm/kg and urine osmolality was 182 mOsm/kg. The patient was discharged with desmopressin 0.1 μg/day and recommended water intake of ≥2.1 l/day.

After 15 days he returned for follow-up with serum sodium of 145 mEq/l, creatinine of 1.6 mg/dl, serum osmolality of 314 mOsm/kg and urine osmolality of 606 mOsm/kg. Clinical examination was unremarkable, except for an early memory deficit and deficiency in retention of information and judgment. A magnetic resonance imaging (MRI) scan carried out 6 months after the surgery only showed mild ischaemic areas at the periventricular region without myelosis.

Discussion

Hypodipsic hypernatraemia is a rare condition characterized by hypertonic dehydration associated with the absence of thirst or with inappropriately low thirst in the presence of sustained and significant hyperosmolality. It is caused by malfunction of the hypothalamic osmoreceptors that regulate thirst [3]. Because these osmoreceptors are anatomically close to those responsible for ADH secretion, the osmoregulation of ADH is usually impaired as well. This defect is limited to the osmoregulation of ADH secretion and usually does not affect neurohypophysis or its regulatory afferents. Therefore, some degree of urine concentration is preserved in these patients [9]. Hypodipsic hypernatraemia may occur in patients with congenital malformations or acquired diseases affecting the anterior hypothalamus, such as tumours, trauma, granulomas, inflammation,
degenerative disorders and brain aneurysms [3]. Aneurysms of the anterior communicating artery are one of the possible causes for the osmoreceptor defect, since this vessel originates in the perforating arteries that are the single blood source for the medial-anterior hypothalamic area [3]. Although the precise anatomical site of injury in patients is unknown, changes in the osmoregulation of thirst and ADH secretion, similar to those seen clinically, were obtained experimentally when structural injuries were performed to the anterolateral hypothalamic area, close to the supraoptic nuclei [9].

The diagnosis of hypodipsic hypernatraemia was confirmed in this case by the association of significant hypernatraemia and absence of thirst in a conscious patient with free access to water. As it usually occurs, a simultaneous partial central diabetes insipidus was present. At ER admission, the presence of renal failure and volume depletion jeopardized this diagnosis. However, it should have been suspected when the patient had polyuria in the presence of hypernatraemia. In fact, the impairment of ADH release usually becomes clear in hypodipsic hypernatraemia only after water loading to correct sodium levels precipitates polyuria, despite the lack of correction of serum osmolality [10]. Diagnosis of partial central diabetes insipidus was confirmed later by measurement of an inadequately low serum ADH in the presence of hypernatraemia, by the inability to concentrate urine and by the increase in urine osmolality after desmopressin administration [3,10].

The prevailing symptoms of hypernatraemia are neurologic. The increased extracellular fluid (ECF) osmolality results in a shift of water from the cells into ECF, causing brain cell dehydration and shrinkage. The severity of neurological symptoms is related to the degree and the rate of serum osmolality increase. Patients with moderate or chronic hypernatraemia may be asymptomatic or show a mild confusional status (and, obviously, thirst, if the thirst mechanism is intact). Usually, hypernatraemic patients present non-specific central nervous system changes, such as nausea and vomiting, muscle weakness, restlessness, irritability, confusion, somnolence and lethargy. The neurological injury can progress in severe cases to seizures, coma and death [1,9–11]. Brain volume contraction can pull and tear intracerebral veins, causing subarachnoid or intracerebral haemorrhages [10]. Haemorrhagic areas were not seen in the CAT brain scan of our patient, but the presence of RBCs in the spinal fluid suggested that cerebral bleeding had occurred at some point. Surprisingly, despite the striking elevation in serum sodium, the patient’s neurological symptomatology did not evolve to seizures or coma, indicating that the development of hyperosmolality was gradual.

Another possible neurological complication of severe hypernatraemia is pontine and extrapontine myelinosi, which may be diagnosed by MRI, performed 2–3 weeks after the development of hypernatraemia [15]. Experimental studies have shown that hypernatraemia may cause brain myelinosi in rats and that the osmotic gradient necessary to produce brain lesions is higher for normonatraemic than for hyponatraemic animals [16]. A late MRI scan did not find lesions indicating myelinosi in the present case. The cognitive deficit remaining in this patient might be related to the neurosurgery or to a hypernatraemia sequela. Neuropsychological evaluations carried out after surgeries of the anterior communicating artery aneurysms found memory problems and other cognitive function deteriorations [17].

Rhabdomyolysis and ARF are other possible complications of severe hypernatraemia [13,14], which effectively occurred in this case. Rhabdomyolysis may aggravate hypernatraemia, because the intracellular breakdown of macromolecules in smaller molecules will promote the shift of water from ECF into muscle cells. ARF was likely caused by the association of rhabdomyolysis and decreased ECF volume. Although the patient was not hypotensive at emergency admission, the history of frequent falls at home (postural dizziness?) and the development of ARF were indicative of volume waste. He weighed 63 kg at the first hospital discharge, but his clinical condition did not allow for his weight to be obtained at re-admission in the ER. It should be noted, however, that the patient must have lost ~30% or more of body weight in free water to achieve such high levels of serum sodium. This degree of volume waste is usually followed by severe hypotension or shock, which did not occur, raising the possibility that the observed hypernatraemia was a consequence of a combination of total body sodium increase and free water loss. The calculation of water deficit in our patient showed a deficit of ~12.5 l and a gain of sodium of ~500 mEq, which means an additional need of free water of ~3.5 l in order to dilute this excess of sodium in the ECF to a concentration of 137 mEq/l [12].

In the treatment of hypodipsic hypernatraemia, either too rapid or too slow approaches may cause significant mortality and morbidity. The brain rapidly triggers protective mechanisms to fight osmotic dehydration. The first adaptive response, occurring within a few hours, is a cellular uptake of sodium, potassium and chloride, minimizing brain volume decrease. The normalization of brain volume is achieved in the next days through an intracellular accumulation of organic osmolytes, but the high osmolality state persists [18]. Because the organic osmolytes cannot be extruded quickly, abrupt corrections of ECF tonicity could result in cerebral oedema, seizures, permanent neurological damage and even death. The current recommendation for hypernatraemia treatment of long or unknown duration is to control sodium in a rate ≤0.5–0.7 mEq/h (12–16 mEq/day) or 10% of natriaemia a day. No more than half of the water deficit should be given during the first 24 h and the rest in the following 2–3 days [9–11]. Additional replacement must be provided to compensate ongoing obligatory fluid losses. If the patient is symptomatic or when hypernatraemia has developed acutely (in hours), the correction rate should be more rapid, not exceeding 1 mEq/l/h [11]. Our patient clearly...
had chronic symptomatic hypernatraemia. The finding of a normal CAT brain scan indicates that adaptive manoeuvres accommodating the brain had already taken place and, therefore, there was risk of cerebral oedema due to water replacement. His sodium decreased 22 mEq/l in the first 24 h (0.92 mEq/h) and ~14 mEq/l/day if we consider the first 3 days of treatment. Although this rate of correction was relatively rapid, the patient did not present evidence of cerebral oedema. Park et al. [7] described a case of hypernatraemia with serum sodium of 206 mEq/l, where the speed of correction was even faster, without inducing neurological complications. Actually, the rate of water replacement in severe hypernatraemia is still controversial. Experimental studies have originated conflicting results, with rapid correction of chronic hypernatraemia causing important brain oedema in rabbits but not in rats [18]. Definitely, there are not enough data available allowing consistent recommendations for the correction of hypernatraemia as severe as observed in the present case.

Other important considerations in water replacement are the route and type of fluid. The oral route should be used preferentially, but the presence of neurological complications frequently obligates the use of i.v. infusions. To achieve a positive water balance and a decrease in serum sodium concentration, the sodium in the fluid used for replacement should always be smaller than the serum sodium concentration if the patient is oliguric and smaller than the sum of urinary sodium and potassium concentration if the patient is polyuric [11]. Only hypotonic solutions, such as electrolyte-free water, 5% dextrose in water, 0.2% sodium chloride and 0.45% sodium chloride, should be used. Because our patient was not oliguric and had some degree of ECF volume contraction, half normal saline was a good initial choice. Subsequently, when he developed polyuria, the urinary electrolytes should have been measured. If urinary sodium concentration was lower than that in the infusion, 0.45% saline would no longer be appropriate and could have worsened hypernatraemia.

The management of hypernatraemic hypodipsia usually involves treatment of central diabetes insipidus to stop water loss. Intranasal desmopressin, parenteral ADH or drugs that increase ADH release, such as chlorpropamide, clofibrate and carbamazepine, may be used in these patients [3,9,10]. The successful long-term treatment of hypernatraemic hypodipsia requires an excellent instruction of the patient to obtain adherence for a strict scheme of daily water intake. The patient should be aware of his/her vulnerability to environmental conditions and oriented to modulate water intake according to body weight changes.

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References


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