Severe hyponatremia due to water intoxication in a child with sickle cell disease: A case report

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Abstract

Water intoxication is a potentially fatal hypo-osmolar syndrome with brain function impairment. Isolated symptomatic excessive ingestion of free water is very rare in childhood. We report a case of acute hyponatremia due to water intoxication without Antidiuretic Hormone (ADH) excess in a child with sickle cell disease. The boy was admitted to our Emergency Department because of new-onset prolonged generalized seizures. Blood test showed hyponatremia, and elevated creatine kinase value; neuroimaging was negative. His recent medical history revealed that on the day before he had drunk about 4 liters of water in 2 hours to prevent sickling, because of back pain. He was treated with mild i.v. hydration with normal saline solution and showed progressive clinical improvement and normalization of laboratory test. Rhabdomyolysis is a rare complication of hyponatremia whose underlying mechanism is still unclear.

Introduction

Hyponatremia is the most common electrolyte disturbance in children. It is defined as serum sodium concentration ([Na+]) < 135 mmol/L and can be associated to hypovolemia, euvolemia, or hypervolemia.

In most cases, hypervolemic or hypotonic hyponatremia results from excessive water intake or water retention. The physiological response to the fall in plasmatic osmolality is the suppression of Antidiuretic Hormone (ADH) release, resulting in increased free renal water excretion and normalization of [Na+]. When water intake is extremely high and exceeds renal free water excretion, then [Na+] lowers.

In case of acute hyponatremia, the rapid decline of [Na+] may overwhelm the adaptive mechanisms of the body, and leads to concentration gradient between extracellular and intracellular compartments, especially in the brain, making it swelling. Children may initially present nausea and vomiting, then headache, lethargy or agitation, seizures, until coma and death.[1]

The most common cause of hypotonic hyponatremia in childhood is ADH excess with free water intake. Isolated symptomatic excessive ingestion of free water is very rare, because healthy children are able to excrete a high volume of dilute urine.

We report a case of acute hyponatremia due to water intoxication without ADH excess in a child with sickle cell disease.

Case Report

A ten-year-old boy with sickle cell disease was admitted to our Emergency Department (ED) because of new-onset prolonged generalized seizures. The collection of his personal history was very

difficult because of his mother's poor language comprehension, anyway the recent medical history revealed back pain the day before, treated with acetaminophen and ibuprofen.

When he arrived to the ED, seizures were over, but he still showed altered state of consciousness with psychomotor agitation alternate with drowsiness; no focal neurological findings were observed. Blood tests revealed pH 7.34 (n.v. 7.35-7.45), pCO2 35.5 mmHg (n.v. 35-45 mmHg), sodium 118 mmol/L (n.v. 136-146 mmol/L), potassium 4.28 mmol/L (n.v. 3.5-5.3 mmol/L), chloride 84 mmol/L (n.v. 97-110 mmol/L), glucose 178 mg/dL (n.v. 70-100 mg/dL), haemoglobin 8.7 g/dL (n.v. 12-16 g/dL), and creatine kinase (CK) 2247 UI/L (n.v. 25-140 UI/L); no alterations on coagulation tests and renal function were observed. HbS was 76%.

Under the suspicion of stroke due to sickling event, he was treated immediately with blood exchange, in order to decrease the HbS rate, and morphine. Nevertheless, head CT scan and magnetic resonance angiography were both negative. The electroencephalogram showed diffuse slowing, mainly on the left posterior side. Abdominal ultrasound and chest X-ray were negative as well.

On the first few hours of observation, the boy maintained an alterated state of consciousness, as we started mild i.v. hydration with normal saline solution (30-40 ml/kg/day). He presented remarkable spontaneous polyuria, with urinary output of about 50 mL/kg/hour. Urine osmolality was 286 mOsm/kg and urinary sodium obtained on spot urine sample was undetectable; plasma osmolality was 274 mOsm/kg.

Asking again his mother about the liquid intake, she finally revealed that on the day before the child had drunk about 4 liters of water in 2 hours to prevent sickling, because of back pain. Serum copeptin result was available 24 hours after hospital admission and was 3.1 pmol/L (n.v. 3-8 pmol/L) showing inhibition of ADH release. This was consistent with symptomatic hyponatremia due to water intoxication.

Soon after admission, fever came, along with increased plasmatic markers of infection, so antibiotic therapy was started. CK rose up to 9490 IU/L until the third day. Mild i.v. hydration was continued with slow normalization of laboratory tests and improvement of both clinical condition and electroencephalogram. Total [Na+] intake in the first 48 hours was 3 mmol/kg/day. Serum [Na+] increase was 17 mmol/L in 48 hours.

The patient was discharged in good condition 12 days after admission, with normal [Na+] and CK values and without any neurological consequence.

Discussion

Water intoxication is a potentially fatal hypo-osmolar syndrome with brain function impairment.

In adults, several cases of voluntary water intoxication have been reported in schizophrenic and anorectic patients.[2] Other papers describe symptomatic hyponatremia due to water intoxication in marathon runners;[3] iatrogenic polydipsia because of misinterpretation of medical advice has been also described.[2,4] Some cases of voluntary overconsumption of water occurred as consequence of water-drinking games,[5] but only one was reported in a child.[6] In childhood, water intoxication affects more frequently infants and toddlers. In particular, several cases have been described in infants fed with formula-milk prepared inappropriately or with hypotonic fluids;[7] in some cases, child abuse by forced water intake played a key-role.[8,9] Moreover, hyponatremia after excessive water intake have been reported in children with enuresis, who had not reduced their drinking habits while on desmopressin therapy.

In our case, voluntary excessive water intake was intended to resolve the supposed sickling episode causing back pain, misunderstanding the physician's recommendations. The boy showed seizures and altered mental status, with alternating irritability and drowsiness. Anyway, such features are typical, but not specific of water intoxication and we firstly referred neurological impairment to ischemic stroke, because of personal history of sickle cell disease. Later on, massive polyuria along with the absence of stroke signs at the neuroimaging made us evaluate more accurately the boy's water intake and led us to the correct diagnosis.

The water-sodium homeostasis was imbalanced due to the high water intake, showing hyponatremia and reduced plasma osmolality as well as compensatory reduced levels of copeptin, which led to reduced urine osmolality. The reduced level of copeptin was confirmatory of water intoxication. Copeptin levels in water and sodium imbalance disorders associated to hyponatremia, such as Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) and cerebral/renal salt wasting, result higher than normal and urine osmolality is consequently also high.[10-12] In our case, the time between water intake and seizures onset was approximately 12-24 hours, as already reported: the time sufficient to precipitate hyponatremic seizures after excessive water intake ranges from 90 minutes to 48 hours.[1,4] Our patient also presented rhabdomyolysis, which is a known, but rare complication of hyponatremia, and whose underlying mechanism is still unclear. Most of literature supports the hypothesis that the fall of potassium level in the muscle due to hyponatremia and hyposmolarity is the leading cause.[13] Other hypotheses suggest drugs, alcohol, and convulsions as factors that possibly induce rhabdomyolysis.[14] Few reports have attributed rhabdomyolysis to the correction of hyponatremia, assuming that the decrease of cell volume following osmolarity increase might result in membrane fragility and enzyme leakage.[13] Our patient presented prolonged seizures, but the lack of temporal relationship with the progressive rise in CK values makes them unlike to be the main cause of rhabdomyolysis: in fact, CK levels continued to rise, peaking on the third day, despite no further seizures were reported. For this reason, we suppose that the main cause for rhabdomyolysis in our patient was hyponatraemia, or its correction by fluid administration.

Fluid management is the mainstay treatment of rhabdomyolysis, hyponatremia and sickling crisis, but by opposite mode. The treatment of rhabdomyolysis involves early and aggressive hydration with intravenous crystalloids alternating with bicarbonate infusion to prevent acute renal failure and death.[14] Moderate intravenous hydration is indicated also in the suspicion of sickling crisis, together with aggressive pain management, though strong evidence on the preferred kind of fluid and route of administration is lacking.[15,16] On the contrary, the management of hyponatremia relies on cautious hydration with isotonic fluids (0.9% saline solution), free water restrictions, diuretics, or a combination of them.[1,2] The goal is slow and cautious correction of [Na+], in order to avoid complications such as pontine myelinolysis. Faster correction with hypertonic 3% saline solution is reserved to patients with status epilepticus or with severe neurological symptoms due to hyponatremia. Hypotonic solutions containing dextrose are not recommended in this conditions as well as desmopressin, due to the unpredictable effect on plasma osmolality and sodium levels.[1,17] Frequent monitoring of serum sodium and plasma osmolality as well as urine osmolality and output are needed, especially in the first 6-12 hours of parenteral hydration.[1] Nevertheless, patients with

self-induced water intoxication typically show massive excretion of dilute urine in the first hours with spontaneous rapid increase of [Na+] (1.5–2.0 mmol/L/h), which is difficult to control.

Recent studies suggest the use of vasopressin receptor antagonists (vaptans) in euvolemic and hypervolemic hyponatremia mainly due to SIADH.[1] Their use is well established in adults with SIADH and needs at least 72 hours to correct hyponatremia. This can be acceptable in patients with chronic hyponatremia as we do not need rapid correction. Therefore vaptans are not recommended in acute hyponatremia. In addition there are few studies in children about the use of vaptans, so to date they are considered off-label in the pediatric age.[1]

Despite the suspicion of sickling event, we managed our patient with mild i.v. hydration with normal saline solution (1 mL/kg/h) and we managed the suspected sickling crisis by blood exchange to avoid fluid overload.

Conclusions

Our case suggests that all the children with alterated consciousness should be checked for serum [Na+], since hyponatremia can lead to severe neurological impairment.

Fluid management of severe hyponatremia due to excess of free water intake should be cautious to prevent rhabdomyolysis and neurological sequelae. The ideal treatment is mild i.v. hydration with normal saline solution, waiting the spontaneous increase of [Na+] by the excretion of dilute urine. Vaptans could provide a future option, but they are still off-label in childhood.

Careful instruction about oral water intake should be provided to all the children with sickle cell disease and their families, in order to prevent excessive water intake.

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