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Hypernatremic hemorrhagic encephalopathy: case report and literature review

Encefalopatia hemorrágica hipernatrêmica: relato de caso e revisão da literatura

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ABSTRACT

Hypernatremia is a common electrolyte disorder in people with impaired thirst control mechanism or access to water, and may lead from minimal disorders until coma. Among the hypernatremia morbidities, central nervous system hemorrhage is uncommon and poorly studied. We report a case involving a patient admitted to the intensive care unit with reduced consciousness level, hypernatremia and head computed tomography scan showing bilateral parenchyma hemorrhage. A literature review of hypernatremia hemorrhagic encephalopathy was conducted.

Keywords: Hypernatremia; Cerebral hemorrhage; Brain diseases

CASE REPORT

A Caucasian 58 years-old male patient with previous high blood pressure and undefined psychiatric disorder was admitted to the Hospital Universitário Professor Edgard Santos of the Universidade Federal da Bahia (HUPES) on February 5, 2010, referred from another service. Twenty days before the admission he was found with reduced sensorial level, oliguria, piuria and increased blood urea nitrogen and creatinine (BUN 180 mg/dL, Cr 5.0 mg/dL). Due to lack of both urinary and sensorial improvement in the previous service, was referred to a higher complexity hospital.

His medical history included systemic high blood pressure and a psychiatric disorder poorly characterized by his family, involving something similar to a bipolar disorder since 14 years-old. Were reported regular use of Haloperidol, Chlorpromazine and Fenergan, prescribed by his treatment doctor. Family members reported that three days before being found with impaired consciousness level, he gone out of home during an agitation crisis.

By admission the patient had precarious general status, was eupneic, had good peripheral perfusion, was discolored +/IV, was restricted to bed and had no signs of trauma. His heart rate was 96 bpm, respiratory rate 24 ipm, and blood pressure 110/70 mmHg. The cardiovascular, respiratory and abdominal examinations evidenced no changes. The neurological examination showed Glasgow 10 (4-1-5), with spontaneous eyes opening, aphasia, and eyes movement when commanded. Tetraparetic, with no signs of hyperreflexia. Isocoric and light reflexive pupils. Other cranial nerves and sensitivity tests were not conducted, as the patient's consciousness level was impaired.

The initial laboratory tests showed hemoglobin 9.5 g/dL, white blood cells count without deviations and platelet counts 210,000/mm^3. Creatinine 5.1mg/dL (reference range: 0.5-1.3 mg/dL), blood urea nitrogen 181 mg/dL (reference

range: < 40 mg/dL). Ionogram revealed sodium 196 mEq/L (reference range: 135-145 mEq/L), potassium 3.3 mEq/L (reference range: 3.5-5.5 mEq/L) and blood gasometry with borderline PO_2, and no metabolic changes.

The patient was transferred to the intensive care unit (ICU) on the 2nd hospitalization day, and put on mechanical ventilation and widened his antimicrobial covering, and then sent to a head computed tomography (CT) scan without administration of a contrast agent which evidenced bilateral cerebellum and external capsule hemorrhage (Figure 1).

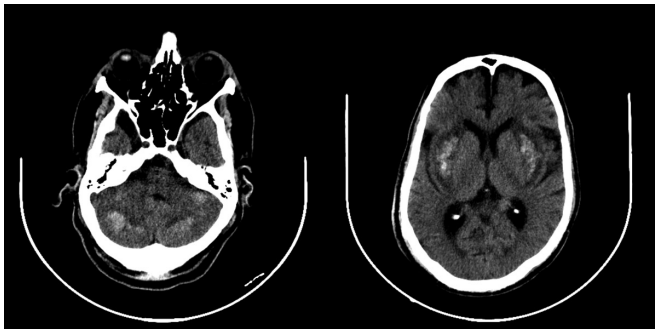
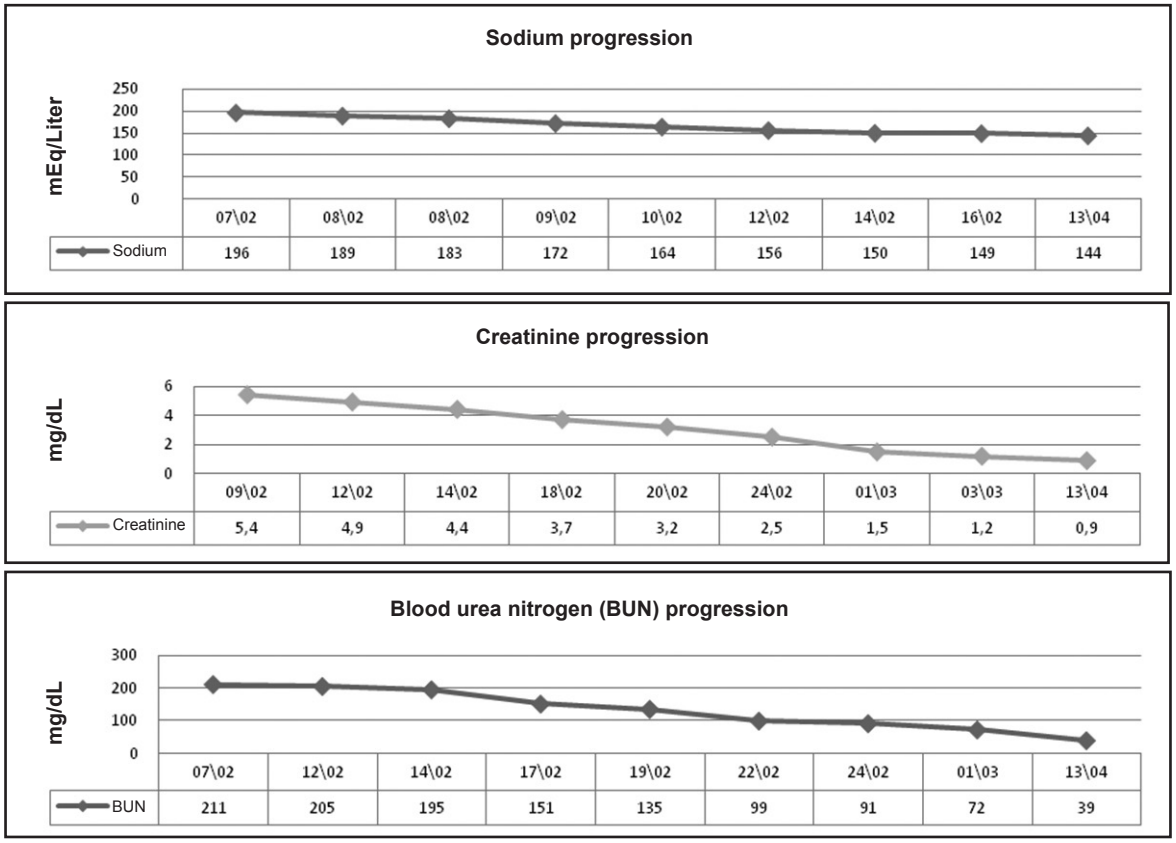


Figure 1 – Head computed tomography scan without administration of a contrast agent evidencing bilateral cerebellum and external capsule hemorrhage and surrounding edema.

The patient progressed in the ICU with improved BUN and creatinine (Graph 1) in addition to increased urinary output following parenteral hydration with crystalloids, with no renal replacement therapy need. After the volume correction, hypotonic solution therapy was started in order to correct the hypernatremia and complying with the daily maximal correction (Graph 1). During the hydroelectrolytic balance correction, and after sedation was withheld, the patient spontaneously opened his eyes and recovered the respiratory drive. Tracheostomized in February 24, was weaned from mechanical ventilation and was discharged from the ICU on March 9, and was discharged from the hospital on April 14, alert and with no neurological deficits.

DISCUSSION

Plasma sodium concentration and serum osmolarity are controlled by the water homeostasis, mediated by thirst, vasopressin and the kidneys. Hypernatremia is a frequent hydroelectrolytic disorder, defined by a sodium plasma concentration above 145 mmol/L.[1] It may be caused either by water and hypotonic fluids loss, inap-



Graph 1 - Sodium, creatinine, and blood urea nitrogen progression

propriate water ingestion, or large hypertonic solutions administration. As it commonly involves more a deficit of water than properly sodium excess, hypernatremia is more frequent in groups with thirst mechanism impairment or restricted access to water. Among the high risk group should be emphasized the impaired mental status subjects, psychiatric patients, those under mechanical ventilation, elderly and children.

Being fundamentally extracellular, sodium contributes for plasma hypertonism leading to water membrane migration. Therefore, its plasma increase leads to hypertonic hyperosmoloarity causing cell dehydration due to water migration to the extracellular space.[1,2] This disorder's morbidities may range from minimal to very serious, including death. This severity is proportional to the disorder's severity and how fast the sodium increases, however it is often difficult to identify the real hypernatremia contribution to the outcome, as other morbidities may be involved.

Hypernatremia and central nervous system hemorrhage

The central nervous system (CNS) is frequently involved in hypernatremia cases. The clinical features described are several, and may include apathy, convulsion and even coma.

Hypernatremia as cause of acute neurological disorder is both well-described, and frequent. However, hypernatremia as cause of CNS hemorrhage is not frequent in the literature. In 1919, Weed and McKibben demonstrated capillary retraction and congestion following hypertonic NaCl infusion in animals, with no hemorrhage evidence.[3] In 1979 Young reported a case of an hypernatremia adolescent after inadvertent hypertonic solution infusion and had seizures and coma. The head CT evidenced small hemorrhages, diffused by the subcortical area, and the necropsy confirmed these findings.[4] In 1997 Han reported on ultrasound and tomography findings in 2 children admitted with neurological signs and hypernatremia.[5] Both patients had similar imagery findings, showing cerebral parenchyma changes with multifocal hemorrhage and hemorrhagic infarction.

Luttrell, in 1958 described three cases in children with hypernatremia and changed consciousness level, ranging from lethargy to coma. The autopsy evidenced central nervous system hemorrhage as predominant pathologic change. Extensive subarachnoidal bleeding, as well as intradural, intracerebral and intraventricular were described in this study. Microscopic examination has shown severe vascular congestion in small and capillary nervous system vessels, with brain tissue pethechiae. As reporting on children admitted with increased sodium and eventually already with consciousness changes, the Luttrell's study did not allow stating that the sodium disorder preceded the hemorrhage, or even caused it.[2]

In 1959, the same author reported on an experimental trial in cats, divided in three groups. On group I, sodium hypertonic solution was injected intraperitoneally, on group II, hypertonic urea solution was injected in the peritoneum, and the group III was the used as control, with part of the group having fluids restriction and the other part peritoneally injected with normal saline solution.[3] It should be remarked that the animals infused hypertonic solutions had no hypertensive peaks during the trial. Marked drop in spinal pressure was identified 60-80 minutes after the hypertonic injection for both intervention groups, and the pressure drop was shorter in the urea group. Cerebral tissue retraction and intracranial hemorrhage were consistently found in similar degrees in both groups, with no hemorrhagic signs in other organs. None of these changes was seen in the control group animals. In six intervention groups animals (4 in the NaCl hypertonic solution and 2 in the urea group) their spinal pressure was maintained for 4 hours by means of cisternal solutions infusion. In this group, the arterial and venous pressure changes were similar to groups I and II without spinal pressure maintenance. The autopsy showed that none of these animals had evidence of intracranial hemorrhage.[2]

Therefore, CNS hypernatremia determined hemorrhage appears to involve several factors. Cell water outflow and slowed sodium transportation between blood and cerebrospinal fluid (CSF) would lead to reduced cerebral and CSF volumes. This results in a negative pressure around the brain tissues, leading to venous and capillary expansion and consequent vessels ruptures.[3] Then, cerebral hemorrhage would result from cerebral retraction inside a rigid structure (the skull) which, associated to negative CSF pressure, would stress the vascular network, and produce hemorrhage from a congested, dilated and consequently fragile capillary network.[2,3] This rational corroborates the necropsy findings where all organs but CNS were spared. The vascular factor as a causative of cerebral hemorrhage would be secondary, and consequent to the CSF pressure reduction. It is admissible, however that vascular injuries in functionally relevant areas may have some primary role on the neurological damage caused by hypernatremia.[2]

Luttrell evidenced a temporal and cause-and-effect relationship between hypernatremia and CNS hemor-

rhage. In addition, by means of this trial it was possible to imply that CSF pressure reduction is fundamental for hemorrhage induction, as it was completely prevented by fluid infusion keeping positive CSF pressure.

It should be noted that in this study by Luttrell, hypernatremia in the intervention group was exclusively induced by hypertonic solution administration (either sodium chloride or urea). Therefore, studies showing that free water or hypotonic fluids loss-induced hypernatremia is a causative of CNS hemorrhage are missing. Additionally, the study had an inappropriate size control group, too small versus the total study animals. However it should be highlighted the consistency of the hemorrhagic findings in the intervention group (48/53; 90.5%). In addition, it would have been interesting measurement of the plasma sodium before and after the intervention, to confirm its levels changes and even to show which sodium levels were associated to cerebral hemorrhage.

In the available studies, the sodium levels associated with intracranial hemorrhage are consistently above 160 mmol/L (Table 1). Most of the studies showing these values, were in children. As the children brains are softer and have higher water content, brain tissue retracts more than adult brains, justifying the higher incidence of hypernatremia induced hemorrhage in younger patients. It is therefore possible that in the adult, the sodium levels associated with CNS hemorrhage are even higher than the commonly described for children.

Interestingly in none of the necropsy findings descriptions was pontine or extra-pontine myelinolisis described, likely because this change is exclusively associated with excessive hyponatremia correction.

We could not find any other hypernatremic hemorrhagic encephalopathy reported in adults (published in English). Therefore, this appears to be the first report in an adult patient.

RESUMO

Hipernatremia é um distúrbio hidroeletrolítico frequente em pessoas nas quais o mecanismo da sede ou o acesso à água está comprometido podendo causar desde morbidades mínimas até coma. Entre as morbidades causadas pela hipernatremia, a hemorragia do sistema nervoso central é infreqüente e pouco estudada. Relatamos um caso de paciente admitido na unidade de terapia intensiva com redução do nível de consciência, hipernatremia e tomografia computadorizada de crânio evidenciando hemorragia intraparenquimatosa bilateral. Foi realizada revisão de literatura de encefalopatia hemorrágica hipernatrêmica.

Descritores: Hipernatremia; Hemorragia cerebral; Encefalopatias

Table 1 – Central nervous system hemorrhage-associated hypernatremia – studies description

Study	Population	Injury (frequency/total)	Sodium level
Cranial ultrasound and CT findings. Han B et al., 2007.[5] 2 cases report	Humans (children)	Intraparenchymal hemorrhage (2/2) Intraventricular hemorrhage (1/2) Capillary and venous congestion (2/2)	180mmol/l 170mmol/l
Hemorrhagic encephalopathy induced hypernatremia I. Luttrell CN, et al.,1959.[2] 3 cases report	Humans (children)	Subarachnoid hemorrhage (3/3) Intraparenchymal hemorrhage (2/3) Hypophysis hemorrhagic necrosis (3/3) Intradural hemorrhage (1/3) Capillary and venous congestion (3/3)	159mmol/l 179mmol/l 180mmol/l
Hemorrhagic encephalopathy induced hypernatremia II. Luttrell CN, et al., 1959.[3] Intervention, 68 cats	Cats	Subarachnoid hemorrhage Intraparenchymal hemorrhage Capillary and venous congestion Subdural hemorrhage	Not reported
Hypernatremia as a cause of intracranial hemorrhage. Roberton NR, et al., 1975.[6] Prospective, 10,072 newborns	Humans (children)	Subdural hemorrhage (4) Subarachnoid hemorrhage (4) Intraventricular hemorrhage (21)	Not reported (no association found)
Hypernatremic hemorrhagic encephalopathy. Young RS, Truax BT, 1979.[4] 1 case report	Human (Adolescent)	Several sucortical hemorrhage (1/1) Capillary and venous congestion (1/1)	172mmol/l

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