CASE REPORT

Iatrogenic water intoxication in a female adolescent with hypopituitarism

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SUMMARY

The authors report a case of a 15-year-old girl with hypopituitarism due to pituitary stalk interruption syndrome diagnosed in the neonatal period. The patient was admitted to the emergency room with impaired consciousness and hypoglycaemia. The day before, she increased her water intake to about 1.5 L to perform a pelvic ultrasound. In the following hours, she developed vomiting and food refusal. Blood analysis revealed hypoglycaemia, hyponatraemia, decreased serum osmolality and normal urinary density. Hyponatraemia and adrenal crisis were managed with a gradual but slow resolution of consciousness and electrolytic balance. This case describes an episode of iatrogenic water intoxication in a patient under desmopressin treatment. Although uncommon, dilutional hyponatraemia is the main complication of desmopressin treatment. We reinforce the importance of patients and caregivers' long-life education for the potential complications of an increase in fluid intake in patients treated with desmopressin.

BACKGROUND

Central diabetes insipidus is a rare disease that results from antidiuretic hormone deficiency. This deficit causes a water balance dysregulation which is usually difficult to manage.[1] The main purpose of chronic management is control of polyuria with the lowest risk of hyponatraemia due to excess water retention. This goal can usually be achieved by administering a long-acting form of antidiuretic therapy and limiting fluid intake to the amounts required to satisfy thirst. Ingesting fluids for any other reason should be discouraged because these patients cannot increase their urine output.[2 3]

Desmopressin, a synthetic analogue of the endogenous antidiuretic hormone, is the drug of choice in diabetes insipidus treatment.[4] Desmopressin is a safe drug; however, water intoxication leading to dilutional hyponatraemia is an uncommon but serious adverse effect.[5] Dilutional hyponatraemia occurs if desmopressin is administered in excess or when fluid intake increases. The clinical presentation of hyponatraemia is often non-specific but may include life-threatening seizures and cardiorespiratory arrest. Patients with mild-to-moderate hyponatraemia may have symptoms such as nausea, confusion and headache, whereas those with severe hyponatraemia will present with vomiting, cardiorespiratory distress, seizures and impaired consciousness. Severe symptoms, as cerebral oedema secondary to the reduced serum osmolality, are most often associated with acute onset hyponatraemia.[6]

This report describes an iatrogenic dilutional hyponatraemia case after a routine medical procedure. We intend to reinforce the importance of patients and parents' education for the potential risks of an increase in fluid intake in patients treated with desmopressin.

CASE PRESENTATION

A 15-year-old girl presented to the emergency room due to impaired consciousness associated with involuntary movements of the limbs.

According to her parents, in the day before, she was submitted to a pelvic ultrasound and was asked to drink about 1.5 L of water. In the following 16 hours, she developed vomiting and food refusal. The pelvic ultrasound was requested to evaluate the ovarian and uterine development in response to oestrogen treatment. There was no recent febrile illness or new drug intake.

The patient had hypopituitarism caused by pituitary stalk interruption syndrome diagnosed in the neonatal period. She was using hormonal replacement treatment with growth hormone (0.021 mg/kg/daily), levothyroxine (112 μg/daily), hydrocortisone (3.8 mg/m^2/daily), lyophilised desmopressin (0.2 mg/daily) and transcutaneous estradiol (50 μg/daily). She was also treated with methylphenidate (18 mg/daily) for attention deficit and hyperactivity disorder.

Familial history was unremarkable.

At prehospital emergency team observation, she was unconscious and presented with hypoglycaemia (34 mg/dL or 1.9 mmol/L). Signs of sphincters incontinence, tongue bite, ocular reversal or sialorrhoea were not present. After subcutaneous glucagon administration, hypoglycaemia resolved, but she maintained impaired neurological state.

In the emergency room, she presented with psychomotor agitation with spontaneous eyes opening. Pupils were isocoric and photoreactive. No apparent focal neurological deficits or meningeal irritation signs were present. She had pale skin and sunken eyes. Blood pressure was 122/51 mm Hg, heart rate 80 beats/min and capillary oxygen saturation 100%. She was afebrile, with immediate capillary filling time, regular breath and normal cardiopulmonary auscultation.

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INVESTIGATIONS

Initial laboratory results revealed blood glucose 66 mg/dL (3.7 mmol/L), hyponatraemia (132 mmol/L), decreased serum osmolality (265 mOsm/kg) and normal urinary density (1.015 kg/L). Creatinine, liver enzymes, blood count and blood gas were normal. C-reactive protein was negative.

Due to persistent psychomotor agitation, despite treatment, and to exclude cerebral oedema, a cranial CT scan was done some hours after admission. CT scan was normal.

TREATMENT

Intravenous hydrocortisone (initial 75 mg bolus and repeated 4 hours later) and fluids were administered. Due to the suspicion of cerebral oedema, 3% sodium chloride and mannitol (0.25 mg/kg) were given. Frequent clinical and analytical monitoring were performed until normalisation of plasma sodium concentration, osmolality and glycaemia.

OUTCOME AND FOLLOW-UP

Eight hours after medical treatment, analytical parameters progressively normalised and the patient regained usual consciousness state. She was discharged with her usual medication and hydrocortisone stress dose. The patient and parents' education about her disease and hormone replacement treatment were reinforced.

DISCUSSION

This case describes an episode of iatrogenic water intoxication in a patient with central diabetes insipidus treated with desmopressin. Water intoxication is a severe disorder with brain function impairment, defined as a hypo-osmolar syndrome resulting from an excess water intake. The dilutional hyponatraemia is caused mainly by an imbalance between the fluid intake and renal water excretion. The translocation of a massive amount of extracellular water into the cells generates an increase in the cellular volume contributing to the development of brain oedema. A variety of neurological signs can occur, including anorexia, emesis, seizures or altered consciousness, depending on the severity and type of onset.[6] In this case, despite clinical signs of brain oedema, CT scan was normal. This fact may be explained by the delay in the CT execution.

In our patient, the excess of water intake without adjustments in desmopressin dosage and the inability to increase urine output lead to water retention and consequently, hyponatraemia. Besides, the acute stress and the inability to increase cortisol production triggered adrenal crisis and hypoglycaemia.

Several cases of water intoxication have been reported among marathon runners, psychiatric patients, perioperative and postoperative excessive fluid infusion, after urological and gynecological interventions. A case of water intoxication secondary to administration of hypotonic fluids in oral rehydration in an infant with gastroenteritis was reported.[7] Some cases of water intoxication in children treated with desmopressin due to nocturnal enuresis, with or without concomitant drugs as an anticholinergic were also described.[8]

Camkurt and Aksu reported three cases of water intoxication after a pelvic ultrasound, although those patients were not treated with desmopressin. They reported a 37-year-old female patient treated with carbamazepine for epilepsy and a 63-year-old woman medicated with ciprofloxacin for urinary tract infection. Both drugs are associated with inappropriate secretion of antidiuretic hormone. In the third case, a 21-year-old female, no other cause besides the increase in water intake was documented.[9]

The authors only found one similar report of a young female with diabetes insipidus treated with desmopressin. Derinoz *et al* described an episode of sudden generalised seizures after drinking nearly 4 L of water before a pelvic ultrasound.[10]

The authors aim to emphasise that the excess water consumption for performing a pelvic ultrasound was required in a hospital setting. In paediatric age, ultrasound is a common imaging modality. To achieve ultrasound imaging, the bladder must be filled with water and patients are asked to drink a few litres of fluid before the procedure. Nevertheless, there are no recommendations about the amount of the fluid intake. In the healthy population, the rapid and excessive intake of water will cause discomfort with an urgent need for voiding.[6] Rarely, the excessive fluid intake in a very short time may cause water intoxication. However, this is particularly important in patients treated with desmopressin.

We intend to alert the medical community for an adequate orientation of the fluid intake for these diagnostic techniques. Additionally, it is essential to carefully evaluate the presence of comorbidities that may justify different and specific procedures. Besides, we reinforce the need for the patient and/or caregivers' education about diabetes insipidus and treatment with desmopressin. Ideally, written instructions must be given for the fluid intake, explaining the importance to drink only for thirst satisfaction. This can be difficult to achieve in infants, children and adolescents whose fluid intake is often motivated by other factors than thirst.

Learning points

- Central diabetes insipidus is a dysregulation of water balance secondary to antidiuretic hormone deficit. Although rare, it is potentially dangerous and often difficult to manage.
- Water intoxication leading to dilutional hyponatraemia is an uncommon but life-threatening complication of desmopressin therapy.
- We reinforce the importance of educating patients and caregivers about the potential risks of fluctuating fluid intake during treatment with desmopressin. Additionally, they should be informed about the signs and symptoms of hyponatraemia.

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