CASE REPORT

Extreme Hypernatremia Combined With Rhabdomyolysis and Acute Renal Failure

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Rhabdomyolysis is a life-threatening condition that involves muscle cell destruction. Among its etiologies, severe hypernatremia is a less common cause. We report a teenage girl with congenital central hypoventilation syndrome and hypothalamus dysfunction syndrome who presented with extreme hypernatremia (sodium, 211 mmol/L) with rhabdomyolysis (creatine kinase, 32,850 U/L) and acute renal failure (creatinine, 6.1 mg/dL) following gastroenteritis with 7-kg weight loss. Rhabdomyolysis subsequently led to acute renal failure and hyperkalemia. Acute hemodialysis was initiated on hospital day 3 for hyperkalemia. This resulted in a 13 mmol/L fall in serum sodium in 3 hours despite using a 156 mmol/L sodium bath, but without the development of cerebral edema or neurological defect. This report highlights an unusual cause of rhabdomyolysis in children and the experience of managing such a difficult clinical situation. [*J Chin Med Assoc* 2009;72(10):555–558]

Key Words: acute renal failure, congenital central hypoventilation syndrome, hypernatremia, hypothalamus dysfunction syndrome, rhabdomyolysis

Introduction

Severe hypernatremia contributes to hyperosmolality and causes cellular dehydration. It may lead to cerebral demyelination, and clinical manifestations range from irritability and lethargy to coma. Hypernatremia is associated with a 15% mortality rate in children,[1] but the rate can go up to 60% in severe cases.[2]

Rhabdomyolysis is also a potentially life-threatening condition that is characterized by muscle necrosis and leakage of muscle constituents into the circulation. The most common contributing factor is crush injury, certain medications, substance abuse, and overexertion. Hypernatremia that leads to rhabdomyolysis and acute renal failure (ARF) has been reported in adults but is rare in children.[3]

Severe hypernatremia is not common, and there are only a few reports on the successful treatment of hypernatremia >200 mmol/L. Here, we share our experience in treating a difficult case and review the relevant literature.

Case Report

A 12-year-old obese girl, 145 cm in height and 60 kg in weight, had complaints of consciousness disturbance. She had been diagnosed with congenital central hypoventilation syndrome (CCHS or Ondine's curse) with hypothalamus dysfunction syndrome and needed noninvasive positive pressure ventilation (bilevel ventilation). She had received regular hormone replacement therapy with thyroxin and desmopressin since the age of 4 years. Due to CCHS, the girl had mild mental retardation with aggressive behavior and required assistance from a caregiver for activities of daily living. She also lacked a thirst drive, probably due to osmoreceptor dysfunction after long-term central apnea and hypoxia. Five days before admission, she had acute gastroenteritis with weight loss of 7 kg. She was referred to the hospital for progressive deterioration of consciousness.

Physical examination was consistent with moderate–severe dehydration. Glasgow Coma Scale score was

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E1V1M5 with floppy limbs. Her blood pressure was 128/75 mmHg, respiration was shallow with a rate of 40 breaths/min, her heart rate was 118/min, and body temperature was 38.3°C. Tea-colored urine was observed in the Foley bag.

Laboratory tests showed a hemoglobin level of 9.8 g/dL, leukocyte count of 5,300/mm^3, platelet count of 48,000/mm^3, blood urea nitrogen of 131 mg/dL, creatinine of 6.1 mg/dL, and serum sodium of 211 mmol/L. Other blood biochemistries were: potassium 3.4 mmol/L, free calcium 0.98 mmol/L, phosphorus 8.7 mg/dL, uric acid 15.5 mg/dL, creatine kinase 32,850 U/L with creatine kinase MB isoenzyme 563 U/L, aspartate aminotransferase 118 U/L, alanine aminotransferase 43 U/L, and lactase dehydrogenase 2,010 U/L. Serum glucose was 214 mg/dL, and blood osmolality was 462 mOsm/kg. Urinalysis showed 9–11 red blood cells per high-powered field, and protein 3+ with positive occult blood 4+ . However, blood and stool cultures were both negative. There was no evidence of trauma or compartment syndrome.

Initially, 0.9% sodium chloride was administered intravenously for hydration, and the serum sodium levels were 198 mmol/L and 180 mmol/L in the 48th and 72nd hours, respectively (Figure 1). Oliguria < 0.5 mL/kg/hr complicated with hyperkalemia (6.6 mmol/L) was noted on the 3rd hospital day even after diuretics and bicarbonate alkalization management. Emergent hemodialysis with high sodium dialysate setting (156 mmol/L) was performed, with a blood flow rate of 100 mL/min and dialysis time of 1 hour. The sodium dropped to 167 mmol/L and serum potassium dropped to 4.4 mmol/L after hemodialysis. The girl did not have seizure attack or signs of brain edema.

The girl underwent another 2 hemodialysis treatments with higher sodium setting from 156 to 140 mmol/L on days 3, 4, 5 and 6. Serum sodium returned to normal range (144 mmol/L) by the 9th hospital day. Consciousness and muscle strength also recovered slowly by the 2nd week. The patient was discharged in the 5th week and received regular hemodialysis for 1 more month. Two months later, follow-up serum sodium was 142 mmol/L, blood urea nitrogen was 47 mg/dL, and serum creatinine was 1.52 mg/dL. Except for mild muscle weakness, the patient's clinical condition recovered to the level before this episode. No significant mental or memory changes were noted. Her renal function was fully restored 4 months later.

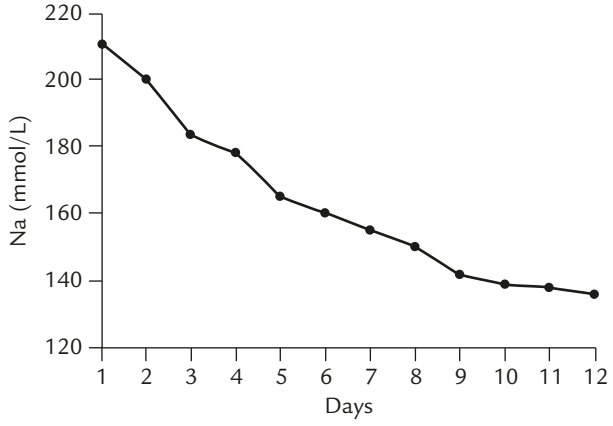

Figure 1. Decrease in serum sodium during admission.

Discussion

Hypernatremia associated with high mortality is defined by plasma sodium level > 150 mmol/L. Hypernatremia is the consequence of water deficit and excessive sodium gain. Children with hypernatremia are estimated to have a 15 times higher risk of mortality than children without hypernatremia.[1] Manifestations of hypernatremia vary, from nonspecific central nervous system changes of nausea, vomiting, muscle weakness, restlessness, irritability, and lethargy to central nervous systemic symptoms of confusion, nystagmus, seizures, myoclonic jerks, and even death. Severe hypernatremia is defined as serum sodium > 160 mmol/L and extreme hypernatremia as > 190 mmol/L.

CCHS is a rare syndrome caused by failure of the autonomic control of breathing. Patients have low sensitivity to hypercapnia and hypoxemia during sleep and wakefulness. Patients with CCHS require lifelong ventilator support during sleep as chronic apnea and hypoxia will cause osmoreceptor dysfunction.[4] Such patients have diminished thirst, and so are at higher risk of developing hypernatremia and dehydration. Recent studies have indicated that the highest mortality is closely related to delayed treatment[1] and not to the severity of hypernatremia. Thus, early detection and aggressive intervention is the backbone of management to prevent unfortunate sequelae.

Rhabdomyolysis is uncommon in the pediatric age group. Elevated serum creatine kinase is the most sensitive and reliable indicator. Red-colored urine due to myoglobinuria can be identified in 74% of cases, but it is not absolutely needed for diagnosis.[5] Our patient was diagnosed according to clinical and laboratory findings. Because rhabdomyolysis is usually caused by crush injury, medications, substance abuse, or overexertion, these etiologies were excluded in our patient by history and physical examination.

Rhabdomyolysis secondary to hypernatremia, such as in this patient, is rarely reported. In 2003, Borrego et al reported 1 case of extreme hypernatremia combined with rhabdomyolysis and ARF, which was caused by hypodipsia and partial central diabetes insipidus after cranial surgery to repair an aneurysm.[6] The exact mechanism of hypernatremia causing rhabdomyolysis is not well known. It is hypothesized that a hyperosmolar state inhibits the electrogenic sodium pump in muscle cells and impairs sodium calcium transport, activating protein kinases and leading to muscle cell lysis.[7] On the other hand, rhabdomyolysis also generates new osmoles in skeletal muscle cells and shifts water from the extracellular to the intracellular compartment. Unfortunately, this further increases serum sodium levels and worsens the hypernatremia.[8]

Rhabdomyolysis has early and late complications. Cell lysis induces hyperkalemia and hypocalcemia, and increases the immediate risk of cardiac arrest. Twenty-five percent of patients have impaired liver function. The most serious complication is ARF, which usually occurs in the initial 12–24 hours after muscle injury. The pathogenesis of ARF includes mechanical obstruction of tubules by myoglobin, direct toxic effect of free chelatable iron on tubules, and hypoperfusion of the kidneys. Patients are at higher risk if creatine kinase level is >16,000 U/L.[9] Fortunately, rhabdomyolysis and the consequent ARF can be completely resolved with early adequate hydration and alkalization. Most renal functions improve within days to 1–2 months.[10,11] According to the diagnostic RIFLE criteria (risk of renal dysfunction; injury to the kidney; failure of kidney function; loss of kidney function; end-stage kidney disease) for ARF in children,[12] our patient had renal loss because renal function did not recover after 1 month but instead had delayed recovery of 4 months.

In the acute hypernatremic state, as in this patient, hemodialysis or peritoneal dialysis, which causes a quick drop in serum sodium, may induce brain edema and seizure.[13] Hence, hemodialysis is associated with high morbidity of neurologic injury and mortality. Moss et al reported the first case of hypernatremia corrected by continuous arteriovenous hemodiafiltration in 1990.[14] McBryde et al demonstrated that using increased sodium or dextrose dialysate could slow the decline in both serum sodium and plasma osmolarity in patients with hypernatremia and hyperosmolality.[15] Hypernatremia was corrected in all of these cases. However, 2 of the 4 reported cases in the above studies used extracorporeal membrane oxygenation (ECMO) support, and 3 of the 4 died due to severe infection or complications of ECMO. The sodium level in these cases ranged from 153 to 180 mmol/L, which was lower than in our patient. To prevent the too-rapid correction of hypernatremia, the sodium level in the dialysate was set to the uppermost level (156 mmol/L was the highest adjustable level). With early and aggressive treatment, the patient did not succumb to hyperkalemia or hypernatremia and survived without neurologic sequelae or other complications.

Extreme hypernatremia (>190 mmol/L) is rare, and only a few cases have been reported. Borrego et al[6] studied patients with extreme hypernatremia >190 mmol/dL from 1990 to 2003. There were 26 patients with sodium levels ranging from 190 to 274 mmol/L. Mortality was 41% and 67% in children and adults, respectively. The most common cause of mortality in adults was the use of saline emetics. Wrong formula concentration was the most common cause in neonates. There was no teenage group like our patient reported to have such a high serum sodium level.

In conclusion, this was a report on a rare case of idiopathic central apnea with hypothalamic dysfunction syndrome that developed extreme hypernatremia and ARF. Extreme hypernatremia is rarely reported in adolescents, and hypernatremia is rarely reported as a cause of rhabdomyolysis. The associated mental retardation and agitated behavior increased the high risk of developing extreme hypernatremia. Prompt and early appropriate intervention with fluid supply and correction of hypernatremia can prevent ARF and death.

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