Case Report

A Fluctuation of Serum Osmolality Inducing Osmotic Demyelination Syndrome

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Osmotic demyelination syndrome (ODS) is an uncommon acute demyelinating process which involves the central nervous system. Rapid correction of chronic hyponatremia with increasing serum osmolality is the most common cause of ODS. We report the first case of an infant with moderate dehydration and initially normal serum Na who developed ODS associated with a fluctuation of serum osmolality. We present the lowest decreasing rate of serum Na level ever reported causing ODS. The fluctuation of serum osmolality in this case expands the list of precipitating causes of ODS in children. The case also highlights the appropriate intravenous fluid for initial rehydration in infant.

Keywords: *Osmotic demyelination syndrome, Infant, Central nervous system, Diarrhea*

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Osmotic demyelination syndrome (ODS) is an uncommon acute demyelinating process which involves pons (central pontine myelinolysis or CPM) and other areas of the central nervous system (extrapontine myelinolysis or EPM). The typical neurological findings are spastic quadriparesis and pseudobulbar palsy. MRI is required for the diagnosis of ODS in most cases.

ODS in children was reported in some conditions such as cytomegalovirus induced hepatitis, liver transplantation as well as in patient with rapid correction of chronic hyponatremia or chronic hypernatremia[1-4]. ODS associated with rapid decreasing of serum Na from normal initial serum Na rarely occurs in children[5]. However, ODS induced by fluctuation of serum osmolality is unknown. We report a previous healthy child with moderate dehydration and initially normal serum sodium who developed ODS associated with fluctuation of serum osmolality.

Case Report

A previously healthy 11-month-old male infant with body weight of 8.7 kilograms presented with a 2-day history of multiple episodes of watery diarrhea and vomiting. Despite being given with oral rehydration solution and antiemetic drug, domperidone, his symptoms persisted. Upon arrival, he appeared drowsy and moderately dehydrated. Neurological examination showed normal findings. Initial serum chemistries showed Na 141 mEq/L, K 4.7 mEq/L, Cl 110 mEq/L, HCO_3 8.1 mEq/L, blood urea nitrogen (BUN) 40 mg/dl, creatinine (Cr) 0.6 mg/dl and glucose 95 mg/dl. Calculated serum osmolality was 301 mOsm/L. Stool examination revealed watery stool without any white blood cells or red blood cells. Stool culture was positive for non pathogenic *E. coli*. Stool for rotavirus was negative. Blood cultures were negative. Initially, 800 ml of D_5 0.3% NaCl was given to correct the dehydration with the infusion rate of 9 ml/kg/hr in the first 8 hours as well as 25 ml of 7.5% $NaHCO_3$ diluted with 25 ml of D_5 water was given to correct the acidosis in the first 4 hours.

Eight hours after admission, he became alert after initial rehydration with serum Na 130 mEq/L, K 3.2 mEq/L, Cl 106 mEq/L, HCO_3 15 mEq/L, BUN 32 mg/dl, Cr 0.5 mg/dl, glucose 106 mg/dl and calculated serum osmolality 277 mOsm/L. Then, he was rehydrated with 700 ml of D_5 0.45% NaCl with KCl 6 mEq/L given in 16 hours. On the first day of treatment, five watery diarrheas were documented; the concurrent loss was

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replaced with 800 ml of milk and oral rehydration solution. Thus, in the first twenty four hours the patient received a total fluid amount of 2,300 ml (264 ml/kg/day) with Na 14 mEq/kg/day, K 0.5 mEq/kg/day and HCO_3 2.7 mEq/kg/day. The patient remained hypokalemia with metabolic acidosis after the treatment (Table 1).

On the second day of admission, the patient became irritable with quadriparetic and gaining weight of 1 kilogram. His neurological exam revealed drowsiness and generalized hypotonia with absent deep tendon reflexes. His cranial nerve functions including ocular movement to all directions and papillary reaction to light were intact. However, unresponsiveness to sound stimulation was documented. Extensor plantar responses were elicited bilaterally. ODS was suspected because of the presence of abnormal neurological function of the central nervous system. The patient received 1,000 ml of D_5 0.3% NaCl with KCL 10 mEq/L and 930 ml of milk and water. On the second day, the patient received Na 5.2 mEq/kg/day, and K 1 mEq/kg/day. The blood chemistry revealed Na 139 mEq/L, K 3 mEq/L, Ca 10 mg/dL, Mg 1.9 mg/dL, BUN 25 mg/dl, Cr 0.5 mg/dl, glucose 85 mg/dl and calculated serum osmolality 289 mOsm/L (Table 1). A computerized tomography (CT) of brain was unremarkable. A lumbar puncture revealed normal cerebrospinal fluid (CSF) with opening pressure of 25 cmH_20. A MRI of brain demonstrated patchy non-enhancing hyposignal T1/hypersignalT2 change with restriction of water diffusion involving bilateral basal ganglia and both cerebellar peduncles. Minimal change was also observed over central pons (Fig. 1). An electroencephalography revealed diffuse slowing of the background activities and slow posterior rhythm for age indicating diffuse cerebral dysfunction. Therefore, the diagnosis of ODS was given. His treatment included baclofen, supportive care and physical therapy. The patient was hospitalized for 3 weeks. He became alert and his spasticity was improved. A quadriparesis with brisk response of all deep tendon reflexes, positive pathologic reflex and bilaterally extensor plantar responses were found prior to being discharged.

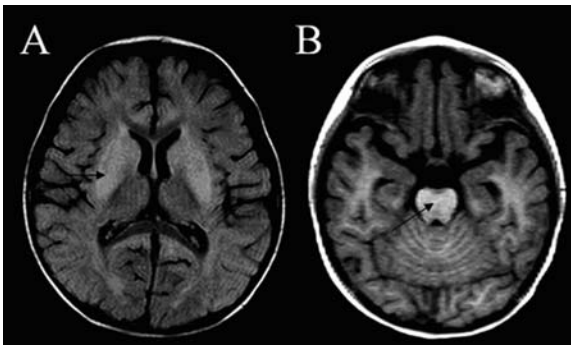

Fig. 1 On hospital day 8, an axial T2-weighted magnetic resonance image demonstrates areas of increased T2 signal intensity within the basal ganglia (A, arrow) and central pons (B, arrow).

His neurological impairment was gradually

Table 1. Laboratory values and intravenous fluid used

Values	Initial	8 hours	24 hours	48 hours
Body weight (kilograms)	8.7	NA	9.7	9.8
Na (mEq/L)	141	130	137	139
K (mEq/L)	4.7	3.2	3.0	3.5
Cl (mEq/L)	110	106	112	113
HCO3 (mEq/L)	8.1	15	16	18
BUN/Cr (mg/dL)	40/0.6	32/0.5	25/0.5	17/0.4
Blood glucose (mg/dl)	95	106	85	90
Serum osmolality* (mOsm/L)	301	277	287	289
Intravenous fluidInfusion rate (ml/kg/hr)	D5 0.3% NaCl plus 7.5% NaHCO 9	D5 0.45% NaCl plus KCL 5	D5 0.3% NaCl plus KCL 4	D5 0.3%NaCl plus KCL 4
Total fluid intake (ml/day)	NA	NA	2,300	1,900

BUN = Blood urea nitrogen; Cr = Creatinine, NA = Not applicable, Serum osmolality* = Calculated serum osmolality

improved. His interaction to the environment and sound stimulations increased with social smile and object fixation at three months of follow-up. Intact extraocular eye movements, facial expression and gag reflex were also noted. The spasticity of all extremities and motor power grade 4 of 5 were documented. The previously positive pathological reflexes disappeared.

Discussion

ODS is a rare acute demyelinating process associated with many conditions. Rapid correction of chronic hyponatremia with increasing serum osmolality is the most commonly precipitating cause of ODS. Shrinking of glia cells, especially oligodendrocytes, as a result of overly aggressive correction of hyponatremia leads to the ODS development. Therefore, correction of hyponatremic state by limiting the rising of serum sodium concentration to 25 mmol/L over 48 hours is recommended to prevent the ODS complication[5]. Rapid decreasing of high serum osmolarity inducing ODS is uncommon in children. Up to the present only 2 reports of ODS in children caused by the osmotic gradient associated with rapid decreasing of serum osmolality include 1) three children with rapid correction of severe hypernatremia of 195 mmol/L to 138 mmol/L within 96 hours, 177 mmol/L to 147 mmol/L within 72 hours and 168 mmol/L to 145 mmol/L within 48 hours[2], 2) a young female with diabetic ketoacidosis after rapid correction of blood glucose from 38.9 mmol/L (700.6 mg/dl) to 8.2 mmol/L (147.7 mg/dl) within 7 hours[3]. A report of a previous healthy young boy with an acute diarrhea episode and ODS, who serum Na declined from 136 mEq/L to 118 mEq/L (4.5 mEq/L/hr), by Greogio et al[5] pointed out that a rapidly changing of normal serum Na in a child may lead to the disease.

In the presented case, the patient developed clinical symptoms with typical MRI findings of ODS after intravenous rehydration therapy for acute diarrhea with moderate dehydration and azotemia. Although the initial serum Na was normal, the serial blood tests demonstrated the rapid decreasing of serum Na followed by increasing serum Na within 24 hours before developing ODS. Strikingly, the lowest level of serum Na in the patient, Na 130 mEq/L, was much higher than 118 mEq/L in the previous reported case by Greogio[5] and the increasing rate of serum Na in the patient, 0.4 mEq/L/hr, was not higher than the recommended rate of 0.5 mEq/L/hr [6, 7]. Therefore, the level of serum Na or the rate of changing serum Na in the patient may not clearly contribute to the ODS development. Since the alteration of serum Na altered the patient's serum osmolality and the patient's serum osmolality was fluctuated by decreasing 24 mOsm/L in the first 8 hours and increasing 10 mOsm/L in the 16 hours after the initial rehydration started, we hypothesize that a fluctuation of serum osmolality caused by a fluctuation of serum Na levels may account for ODS development in this patient.

Other possible causes of ODS in this patient need a discussion. Several conditions including cytomegalovirus hepatitis[2], diabetic ketoacidosis[3], liver transplantation[8], severe liver disease[9], have been associated with ODS in children. Apparently, these reported conditions were not detected in the presented patient. A decreasing rate of 15 mg/dl of BUN in 24 hours should not attribute to ODS, since urea is osmotically ineffective solute. In addition, the initial level of BUN in this patient did not exceed 175 mg/dl as being a common cause of disequilibrium syndrome in new dialysis patients[10].

Acute diarrhea with moderate to severe degree dehydration remains the common problem in children especially in developing countries. Since the losing of extracellular fluid in children with diarrheal dehydration up-regulates antidiuretic hormone (ADH) production; the increasing ADH production makes these children vulnerable to hyponatremia by impairing free water clearance. Thus, expanding extracellular volume with 20-40 ml/kg of isotonic saline in the first hour is recommended to correct hypovolemia in near-shock patient[9,10] and to prevent acute iatrogenic hyponatremia[11]. The approach will potentially prevent the fluctuation of serum osmolality and possibly prevent the ODS development. To the best of our knowledge, the presented case is the first case report of an infant with initial normal serum Na who developed ODS associated with a fluctuation of serum osmolality and the lowest decreasing rate of serum Na level ever reported in children. The case also highlights that choosing appropriate intravenous fluid for initial rehydration in infant with diarrhea is essential and possibly prevents the complication. The fluctuation of serum osmolality in this case expands the reported list of precipitating causes of ODS in children.

In summary, this is the first case report of a fluctuation of serum osmolality inducing ODS in an 11-month-old previously healthy infant with acute diarrhea and moderate dehydration. Awareness of the condition with appropriate initial rehydration in infants with acute diarrhea and dehydration may prevent this catastrophic

event.

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รายงานผู้ป่วยเด็กที่มีภาวะออสโมติกดีมัยอีลีเนชั่นจากการขึ้นลงของซีรัมออสโมล

สุขเกษม โฆษิตเศรษฐ, ศุกระวรรณ อินทรขาว, วนิดา เปาอินทร์, อนันต์นิตย์ วิสุทธิพันธ์

ภาวะออสโมติกดีมัยอีลีเนชั่นเป็นภาวะที่มีการทำลายเซลล์ประสาทชนิดโอลิโกเด็นโดรไซท์ที่พบไม่บ่อย มักเกิดจากการรักษาภาวะโซเดียมในเลือดต่ำอย่างรวดเร็ว ระดับโซเดียมที่สูงขึ้นอย่างเฉียบพลัน ทำให้เซลล์ประสาทเหี่ยว สาเหตุที่พบได้น้อยมากคือการลดลงของระดับโซเดียมในเลือดจากระดับปกติอย่างรวดเร็ว รายงานนี้แสดงภาวะออสโมติกดีมัยอีลีเนชั่นจากการเปลี่ยนแปลงของระดับซีรัมออสโมลในผู้ป่วยเด็กที่มีภาวะท้องเสียเฉียบพลัน ร่วมกับการขาดน้ำระดับปานกลางที่มีระดับโซเดียมในเลือดตั้งต้นอยู่ในเกณฑ์ปกติการเปลี่ยนแปลงระดับโซเดียมลงและขึ้นด้วยอัตรา 0.4 มิลลิอิควิวาเลนท์/ลิตร/ชั่วโมง เป็นอัตราการเปลี่ยนแปลงโซเดียมในเลือดที่ต่ำที่สุดที่มีรายงานในปัจจุบัน รายงานนี้แสดงถึงความสำคัญในการเลือกสารน้ำที่เหมาะสมในการรักษาผู้ป่วยที่มีการขาดน้ำระดับปานกลางถึงรุนแรง