EXTRAPONTINE MYELINOLYSIS IN A NINE-YEAR-OLD CHILD*

*Fadıl Öztürk MD**, Semih Görk MD***, Murat Aydın MD****
*Lütfi İncesu MD*****, Kemal Baysal MD******

SUMMARY: Öztürk F, Görk S, Aydın M, İncesu L, Baysal K. (Department of Pediatrics, Pediatric Surgery, and Radiology, Ondokuz Mayıs University Faculty of Medicine, Samsun, Turkey). Extrapontine myelinolysis in a nine-year-old child. Turk J Pediatr 1998; 40: 579-584.

Extrapontine myelinolysis in the pediatric age group is very rare. We report a nine-year-old girl with the classical clinical syndrome of pontine and extrapontine myelinolysis following liver trauma due to a traffic accident. She was referred to our hospital for further investigation of convulsions due to severe postoperative hyponatremia. She had no hypoxic event or other identifiable cause for the neurological symptoms. Neurological deterioration began about two days after correction of hyponatremia and followed a period of temporary improvement in hyponatremic encephalopathy. Diagnosis of extrapontine myelinolysis was confirmed with the identification of typical features on magnetic resonance imaging. The rapid correction of hyponatremia seemed the most likely cause since other biochemical tests including liver function tests were all within normal ranges. The long term clinical outcome was good. It is important to carefully monitor the rate of correction in electrolyte disturbances, and to consider the individual variation in response to therapy. *Key words: child, extrapontine myelinolysis, hyponatremia.*

Central pontine and extrapontine myelinolysis (CPM/EPM), also referred to as osmotic demyelination syndrome (ODS), is a demyelinating disease. Although occurring anywhere in the brain, it mainly involves the basis pontis[1-3]. There is controversy over its pathogenesis but recently increasing clinical and experimental evidence has shown that it is the result of a rapid or over-correction of hyponatremia[2,4,5]. It was also reported that ODS is associated with other states of hyperosmolality, such as hypernatremia, hyperglycemia or azotemia[6,7]. The majority of patients are adults, with children being affected only occasionally four cases have been published from 1987 to present. Children generally have

* From the Departments of Pediatrics, Pediatric Surgery, and Radiology, Ondokuz Mayıs University Faculty of Medicine, Samsun.

** Assistant Professor of Pediatrics, Ondokuz Mayıs University Faculty of Medicine.

*** Research Assistant in Pediatric Surgery, Ondokuz Mayıs University Faculty of Medicine.

**** Associate Professor of Pediatrics, Ondokuz Mayıs University Faculty of Medicine.

***** Assistant Professor of Radiology, Ondokuz Mayıs University Faculty of Medicine.

****** Professor of Pediatrics and Pediatric Cardiologist Ondokuz Mayıs University Faculty of Medicine.

an underlying disease such as adrenal insufficiency, brain tumor, liver disease or malnutrition[1]. Almost all pediatric cases reported to date had a central pontine demyelination.

We herein report a case of ODS with extrapontine involvement which developed after the treatment of severe hyponatremia and resolved afterwards.

Case Report

A nine-year-old girl was admitted to our pediatric emergency department with a complaint of seizure. As we were informed by the referring hospital and the mother of the patient who was a nurse, the patient had undergone an exploratory laparotomy following a traffic accident. A six-to-seven-cm-long laceration on the capsule of the right lobe of the liver and also a retroperitoneal hematoma were observed at surgery. She did well early after surgery but complained of headache, nausea and vomiting on the fifth postoperative day. The first generalized seizure appeared on the sixth day, lasted less than 10 minutes, and could be controlled by diazepam. Serum sodium concentration was 115 mmol/L. A replacement therapy was started, a second seizure occurred 12 hours later, and she was referred to our hospital for further investigation.

Past history was unremarkable for the patient and the family.

On examination, she was unable to cooperate but responded to verbal stimuli by opening her eyes. Temperature was 36.3 °C, respirations 24/min, pulse 80 beats/min and blood pressure 110/70 mmHg. There was a sutured incision on the forehead, and two drains were on the right side of the median incision draining the perihepatic region of the laceration and the cave of Douglas. On neurological examination, pupils were dilated and reacted normally to light both directly and consensually. The discs and fundi were normal. No lateralizing features were present. Deep tendon reflexes were symmetric and hypoactive and both plantar responses were extensor. The rest of the physical examination was unremarkable.

Urine density was 1010 and sodium in urine was 20 mmol/L. The hematocrit value was 29 percent, hemoglobin 9.9 g/dl, and WBC count 9,000/mm^3. Blood analysis revealed: serum sodium 111 mmol/L, potassium 4.6 mmol/L, ALT 45 IU, AST 50 IU and PaO_2 85 mmHg. Cranial computed tomography (CT) scan was normal. Cerebrospinal fluid analysis (CSF) disclosed no abnormalities and its culture was negative.

Treatment for hyponatremia was initiated with a fluid containing 0.9 percent sodium chloride with 5 percent glucose at a rate of 80 ml/h (1.4 m^2 body surface). Serum sodium level was 115 mmol/L after eight hours. Infusion of the same fluid was continued, and after an additional eight hours, her serum sodium was 125 mmol/L. The intravenous fluid was changed to 0.45 percent sodium chloride

with 5 percent glucose, and 27 hours after the admittance serum sodium was 142 mmol/L. By the 12th hour her general condition seemed to improve, she became cooperative and was able to talk. However, after 48 hours she became unconscious and developed persistent convulsions, affecting the left arm and the left side of the face, which were irresponsive to anticonvulsive therapy. Deep tendon reflexes were hyperactive and plantar reflexes were bilaterally extensor.

A cranial CT scan on day four revealed minimal, diffuse cerebral edema. CSF analysis on the same day was normal. Fifteen days later, magnetic resonance imaging (MRI) of the brain revealed a normal pons, but there were multiple millimetric foci of increased signal intensity in the frontoparietal periventricular white matter bilaterally on T2 weighted images (Figs. 1a, 1b).

She received intensive supportive therapy while she was comatose during five weeks. Myoclonic seizures localized to the left side of the body were partially controlled. She began to recover dramatically starting from the fifth week. When she was discharged on the 46th day of hospitalization she was able to understand verbal commands, reach her head with her hand and walk with help, although ataxic. She was making hoarse sounds (hypophonia) and suffering from a prominent dysphagia. Pharyngeal reflexes were bilaterally elicitable. Deep tendon reflexes were hyperactive on the left and normal on the right side. Plantar reflexes were bilaterally extensor.

When she was reevaluated two weeks later she was able to walk without help and her speech was dysphasic. She had less dysphagia as stated by her mother.

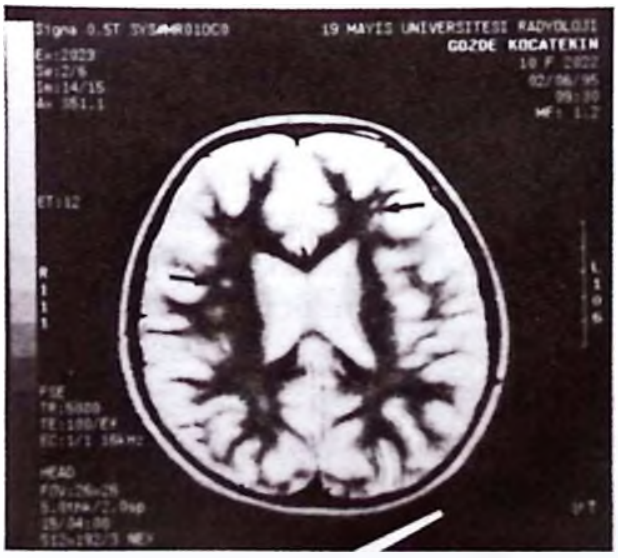

Fig 1a

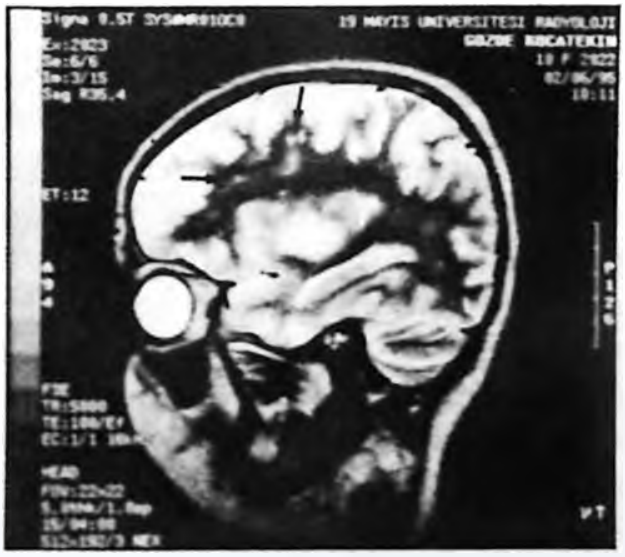

Fig 1b

Fig. 1: Axial (a) and sagittal (b) T2-weighted MR images showing high-signal intensity foci in the frontoparietal periventricular white matter areas (arrows).

Despite carbamazepine therapy she was still suffering from short duration convulsions affecting the left side of the face and the left arm two or three times a day. The convulsions and dysphasia were continuing one month after discharge.

Discussion

Hyponatremia causes a generalized metabolic encephalopathy which present as headache, nausea, vomiting, irritability, restlessness, lethargy, confusion, weakness, malaise, and seizures. These symptoms can usually be reversed with correction of the sodium deficiency[8]. However, the treatment of hyponatremia is controversial because of the risk of causing ODS. Controlled studies in animals have shown myelinolysis following rapidly corrected hyponatremia but not with uncorrected hyponatremia[9,10], although some authors have proposed that uncorrected hyponatremia can itself lead to ODS[11]. Although there is no agreement on exactly how fast an increase in serum sodium is safe, animal studies and clinical trials showed that a rise of greater tah 12 mmol/L per 24 hours and 25 mmol/L per 48 hours carries a danger of causing myelinolysis. The duration of treatment may be important, and a rate of 12 mmol/L per day may be too rapid if continued for two or three days. A general consensus is that the patient not be made hypernatremic[2,5,12].

The pathogenesis of myelinolytic lesions is obscure. It has been suggested that a rapid increase in serum sodium causes an osmotic injury to the endothelium, resulting in the release of myelinotoxic factors and/or the production of vasogenic edema[1,2]. The main pathological event is the destruction of myelin sheaths, but axons and neurons are relatively spared. The lesions are generally symmetrical and multifocal, and tend to involve the areas of white matter where there is a wide zone of conjunction between the gray and white matters[1,5]. Shortly after the correction of hyponatremia (approximately 2-6 days), as in our case, following a transient improvement which parallels the correction of the electrolyte disturbance, a progressive neurological syndrome develops reflecting the dysfunction of white matter of pontine and/or extrapontine sites including internal capsule, basal ganglia and cerebellum. Symptoms of pseudobulbar palsy such as dysphasia, changes in corticospinal reflexes, tetraparesis or tetraplegia, ophthalmoparesis, changes in pupils, convulsions, tremors, incontinence and coma may occur. It is usually fatal. If the patients survive, they may suffer from neurological deficits as severe as akinetic mutism or from less severe sequelae like dysphasia[1,2,12,13].

Although the majority of patients have been diagnosed at autopsy, antemortem diagnosis can also be achieved. Clinical suspicion is supported by radiologic studies. Especially during the early course of the disease, a CT scan may be

normal. Magnetic resonance imaging is more sensitive in diagnosis, showing prolonged T1 and T2 relaxation times in affected regions[14]. Numerous cases in the literature were diagnosed solely according to the typical clinical findings and course of the disease[3,12].

In our patient a clinical picture displaying the typical findings of ODS developed postoperatively following the correlation of hyponatremia. There were periventricular and subcortical multiple foci on MRI in accordance with ODS. On the basis of clinical findings, clinical course and MRI, a diagnosis of ODS was established. It may be proposed that the extrapontine lesions seen in the presented case could be delayed, post-hypoxic demyelination rather than EPM associated with an increase in serum sodium from hyponatremic levels. Although both conditions have superficial similarity such as a biphasic course of illness, there are distinct differences between myelinolysis and delayed, post-hypoxic demyelination. Neurological deterioration due to myelinolysis usually starts earlier and progresses more rapidly than that following hypoxia. In myelinolysis extrapontine lesions are symmetrical and multifocal, as in the presented case, not diffuse as in delayed, post-hypoxic demyelination. Our patient had no evidence of respiratory arrest or hypoxia. Respiratory difficulty during hyponatremic seizures is unlikely to lead to severe cerebral anoxia[5].

In children, there are reported cases of ODS in association with liver disease. Although there was a laceration on the capsule in our patient we could not detect any injury to the parenchyma of the liver, and the liver enzymes were normal. In view of these reasons, the most rational factor to clarify the pathogenesis of EPM in our patients seems to be the rapid correction of hyponatremia.

In our clinics, rapid correction of hyponatremia is not an accepted approach, and hypertonic saline is seldom preferred for therapy. Thus, the initial intravenous fluid for this patient was 0.9 percent sodium chloride with 5 percent glucose. After 16 hours of follow-up, when the sodium level was 125 mmol/L, the sodium was decreased to half of the initial content. Despite this reduction there was a 31 mmol/L rise in the sodium level at the 27th hour of hospitalization. Such an unintended rise can sometimes be encountered due to individual variability in patients' response to therapy.

In conclusion, a patient with hyponatremia is at risk of rapid correction of hyponatremia as well as of the danger of hyponatremia itself.

REFERENCES

1. Fishman MA. Disorders primarily of white matter. In: Swaiman KF (ed). Pediatric Neurology. Principles and Practices Vol. 2. St. Louis: CV Mosby Co; 1989: 755-775.

2. Sterns RH, Riggs JE, Schochet SS Jr. Osmotic demyelination syndrome following correction of hyponatremia. N Engl J Med 1986; 314: 1535-1542.

3. Ayus JC, Krothapalli RK, Arieff AI. Treatment of symptomatic hyponatremia and its relation to brain damage. A prospective study. N Engl J Med 1987; 317: 1190-1195.
4. Ayus JC, Krothapalli RK, Armstrong DL. Rapid correction of severe hyponatremia in the rat: histopathological changes in the brain. Am J Physiol 1985; 248: F711-F719.
5. Laureno R, Karp BI. Pontine and extrapontine myelinolysis following rapid correction of hyponatraemia. Lancet 1988; 1: 1439-1441.
6. McComb RD, Pfeiffer RF, Casey JH, Wolcott G, Till DJ. Lateral pontine and extrapontine myelinolysis associated with hypernatremia and hyperglycemia. Clin Neuropathol 1989; 8: 284-288.
7. Esforzado N, Poch E, Cases A, Cardenal C, Lopez-Pedret J, Revert L. Central pontine myelinolysis secondary to frequent and rapid shifts in plasma glucose in diabetic hemodialysis patient. Nephrol Dial Transplant 1993; 8: 644-646.
8. Mulloy AL, Caruana RJ. Hyponatremic emergencies. Med Clin North Am 1995; 79: 155-168.
9. Kleinschmidt-DeMasters BK, Norenberg MD. Rapid correction of hyponatremia causes demyelination: relation to central pontine myelinolysis. Science 1981; 211: 1068-1070.
10. Illowsky BP, Laureno R. Encephalopathy and myelinolysis after rapid corection of hyponatraemia. Brain 1987; 110: 855-867.
11. Tien R, Arieff AI, Kucharczyk W, Wasik A, Kucharczyk J. Hyponatremic encephalopathy: is central pontine myelinolysis a component? Am J Med 1992; 92: 513-522.
12. Lohr JW. Osmotic demyelination syndrome following correction of hyponatremia: association with hypokalemia. Am J Med 1994; 96: 408-413.
13. Arieff AI. Hyponatremia, convulsions, respiratory arrest, and permanent brain damage after elective surgery in health women. N Engl J Med 1986; 314: 1529-1535.
14. Morlan L, Rodriguez E, Gonzales J, Jimene-Ortiz C, Escartin P, Liano H. Central pontine myelinolysis following correction of hyponatremia: MRI diagnosis. Eur Neurol 1990; 30: 149-152.