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Case Report

The Treatment of Cerebral Salt Wasting with Fludrocortisone in a Child with Lissencephaly

Lissensefalili Bir Çocukta Gelişen Serebral Tuz Kaybının Fludrokortizon ile Tedavi Edilmesi

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ABSTRACT

Hyponatremia is the most frequent electrolyte disorder in critically ill neurological patients. The major differential diagnoses in this situation are the syndrome of inappropriate antidiuretic hormone secretion, marked by inappropriate retention of free water, and cerebral salt wasting, characterized by excessive urinary loss of sodium and resulting in polyuria and extracellular volume contraction. Cerebral salt wasting is a syndrome of hyponatremia due to increased urine output and excessive natriuresis described in patients with central nervous system disease. Although cerebral salt wasting has been well described in neurosurgical patients, data regarding pediatric patients is sparse. We present a 34-month-old boy with lissencephaly who developed cerebral salt wasting after brain biopsy. The patient was treated with hypertonic saline and multiple antiepileptic drugs. Fludrocortisone supplementation effectively treated cerebral salt wasting.

KEYWORDS: Cerebral salt wasting, Child, Fludrocortisone, Hyponatremia, Lissencephaly

ÖZ

Hiponatremi, ağır nörolojik hastalığı olanlarda en sık görülen elektrolit bozukluğudur. Bu durumun ayırıcı tanısında iki major bozukluk uygunsuz antidiüretik hormon salınımı ve serebral tuz kaybıdır ki, birincisinde uygunsuz su retansiyonu varken, ikincisinde ise poliüri ve ekstraselüler volüm kontraksiyonu ile sonuçlanan idrarla aşırı tuz kaybı sözkonusudur. Serebral tuz kaybı beyin cerrahisi hastalarında iyi tarif edilmesine karşın, pediatrik hastalardaki durumu ile ilgili yeterli veri bulunmamaktadır. Biz bu makalede, lissensefalili 34 aylık erkek çocuk hastada beyin biyopsisi sonrasında gelişen serebral tuz kaybını anlatmaya çalıştık. Hasta hipertonik salin solüsyonu ve çoklu antiepileptiklerle tedavi edildi. Serebral tuz kaybı ise fludrokortizon ile etkili biçimde tedavi edildi.

ANAHTAR SÖZCÜKLER: Serebral tuz kaybı, Çocuk, Fludrokortizon, Hiponatremi, Lissensefali

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INTRODUCTION

Hyponatremia is the most frequent electrolyte disorder in critically ill neurological patients (2). The major differential diagnoses in this situation are the syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH), marked by inappropriate retention of free water, and cerebral salt wasting (CSW), characterized by excessive urinary loss of sodium and resulting in polyuria and extracellular volume contraction (8,11). Differentiation of the CSW syndrome from SIADH is essential because of the completely different principles of treatment in these two pathologic processes and because inadequate management can result in unnecessary hyponatremia-related morbidity in unrecognized patients with CSW (1,4). The treatment of CSW consists of volume for volume replacement with 0.9% and/or 3% sodium chloride (6,10). High-dose mineralocorticoid administration is of benefit in a few patients, and the use of the mineralocorticoid fludrocortisone to treat cases of CSW has only been reported in isolated pediatric cases (7,11). Here we describe a 34-month-old boy with lissencephaly who developed CSW after the brain biopsy for a suspicion of tumor, and discuss the efficacy of fludrocortisone treatment.

CASE REPORT

A 34-month-old boy was admitted to a community hospital with generalized tonic-clonic seizure that had developed during the neonatal period. His magnetic resonance imaging (MRI) showed a frontotemporal mass, and he underwent a frontotemporal craniotomy. Only a biopsy could be taken during surgery. He was transferred to pediatric intensive care unit of Ankara Dışkapı Pediatric Disease Education and Investigation Hospital for further management two days later because of status epilepticus and increased lethargy.

On arrival to our pediatric intensive care unit, the patient's physical examination was remarkable for his obtunded mental state and the Glasgow Coma Scale was 6. Initial vital signs were heart rate of 128/min, respiratory rate of 32/min, central temperature of 37.8° C and blood pressure of 95/62 mm Hg. His weight was 9.1 kg (< 3rd percentile), height 94 cm (3-10th percentile) and head circumference 48.5 cm. Laboratory tests performed routinely on admission revealed: serum sodium 134 mEq/L; potassium 4.5 mEq/L; chloride 103 mEq/L; urea 18 mg/dl; and creatinine 0.3 mg/dl. The peripheral blood count showed the following: hemoglobin 11.2 g/dl; white blood cells 9300/mm^3; and platelets 325000/mm^3. We continued the treatment of phenobarbital, pheytoin, and carbamazepine, and started a midazolame infusion (2 to 10 μcg/kg/d) to control the seizures. His MRI was reevaluated and showed a frontotemporal mass (52X42X35 mm) extending to the calvarium, congenital agenesis of corpus callosum, and pachygyria (Figure 1A,B,C). The pathological examination of the biopsy excluded a tumor and we then made a diagnosis of lissencephaly. On the 3rd day of hospitalization, his urine output had increased to 13.8 ml/kg/h. Serum sodium was 124 mEq/L, urine sodium was 146 mEq/L, and urine density was 1006. The ADH level was 5.9 pg/ml (0-8.8 pg/ml, Ankalab Medical Laboratories, Ankara, Turkey). A diagnosis of CSW was made. We managed the volume depletion and hyponatremia with intravenous fluids 24 mEq/kg/d of sodium in the form of 0.9% and 3% NaCl, but we could not decrease the urine output and natriuresis. We then initiated oral fludrocortisone at 0.05 mg every 12 h. Five days later, we increased the dosage of fludrocortisone to 0.1 mg every 12 h. On the 17th day of the fludrocortisone therapy we were succeed in controlling the polyuria (3.8 ml/kg/d) and the natriuresis (42 mEq/L). Meanwhile, we achieved stopping his seizures and stopped the midazolam infusion.

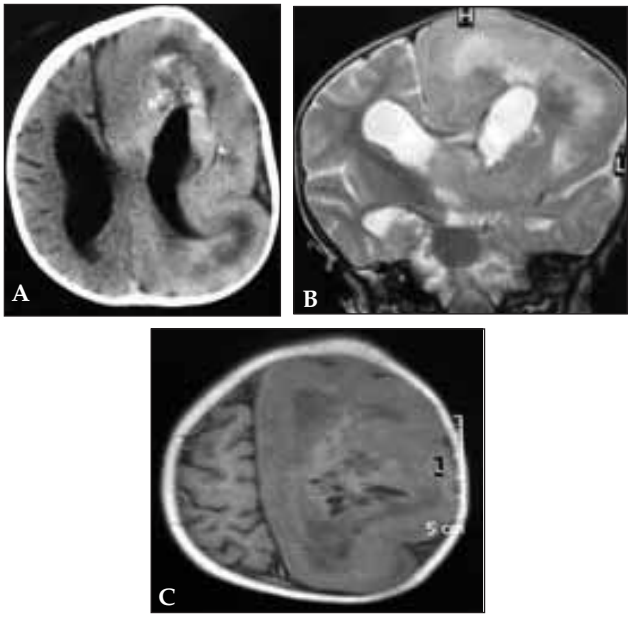

Figure 1A, 1B and 1C: *MRI shows frontotemporal mass extending to the calvarium, congenital agenesis of corpus callosum, and pachygyria.*

DISCUSSION

CSW, a clinical syndrome characterized by hyponatremia, excessive natriuresis, volume depletion and clinical response to volume and salt replacement, occurs in patients with head trauma, central nervous system surgery, tumor or meningitis (4,9). This condition is completely distinct from SIADH. The wrong diagnosis could lead to inappropriate fluid restriction and worsen the hypovolemia (6,10). Clinicians must therefore be aware of this entity and the clinical features that distinguish CSW from SIADH (Table I). The major difference between CSW and SIADH is that CSW involves renal salt loss, resulting in hyponatremia and extracellular fluid volume decrease, whereas SIADH involves physiologically inappropriate secretion of ADH or increased renal sensitivity to ADH leading to renal conservation of water and euvolemic or hypervolemic hyponatremia (3).

Table I: Differential diagnosis of CSW and SIADH.

	CSW	SIADH
Weight	↓	↑
Clinical dehydration	+	-
Plasma sodium concentration	↓↓	↓
Urine sodium concentration	↑↑	variable
Urine flow rate	↑↑	↓
Net sodium loss	+++	±
Plasma ANP concentration	↑	↑
Plasma renin activity	↓	↓
Plasma aldosterone concentration	↓	↓
Plasma ADH concentration	↓	↑
Response to saline infusion	correct	temporary and limited

Aggressive replacement of urine salt and water losses using 0.9% or 3% sodium chloride is the cornerstone of treatment of CSW (10). On the other hand, the event sometimes becomes prolonged as in our patient and replacement of urine salt and water losses cannot solve the problem. The use of fludrocortisone in patients with prolonged of urine salt and water losses can treat the CSW and it was first reported in the 1980s in adults with head injury, and single case reports of its use in pediatric cases have appeared sporadically (6,7,10). This treatment was considered because of the associated hormonal pattern of the suppressed renin-angiotensin system in CSW (6,10). Kappy et al., Taplin CE et al., and Sakarcan A et al. reported the only pediatric CSW cases with subdural bleeding, brain tumors, and tuberculous meningitis, that responded to fludrocortisone acetate (6,10,11). Our patient demonstrated that mineralocorticoid supplementation could effectively control the natriuresis and excessive urine output secondary to brain biopsy in a child with lissencephaly.

Our case suggests that CSW can also be observed after little interference to brain and that lissencephaly and fludrocortisone supplementation seems to be safe and effective treatment for CSW.

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