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Brief report

The role of fludrocortisone in a child with cerebral salt wasting

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Abstract. Cerebral salt wasting (CSW) is a syndrome of hyponatremia due to excessive natriuresis described in patients with central nervous system insult. We present a 29-month-old black male with tuberculous meningitis who developed CSW with depressed mineralocorticoid activity. The patient required hypertonic saline and inotropic support. Mineralocorticoid supplementation effectively treated CSW.

Key words: Cerebral salt wasting – Hyponatremia – Tuberculous meningitis – Fludrocortisone

Introduction

Hyponatremia has long been recognized as a potentially serious metabolic consequence of central nervous system (CNS) insult in children. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) has until recently been thought to be responsible for the majority of cases of hyponatremia developing after CNS insult [1]. It has become evident that a distinct entity of excessive urine output and natriuresis, termed cerebral salt wasting (CSW), can cause hyponatremia in some children after cerebral insults such as trauma or infection [2–4]. Inappropriate atrial natriuretic peptide (ANP) secretion has been proposed as a possible pathogenetic mechanism for CSW in pediatric patients with subarachnoid hemorrhage and tuberculosis meningitis (TBM) [2–4]. The treatment of CSW consists of volume for volume replacement with 0.9% and/or 3% sodium chloride [3]. High-dose mineralocorticoid administration is of benefit in a few patients [3, 5, 6]. We describe a 29-month-old black male with TBM who developed CSW, and discuss the efficacy of high-dose mineralocorticoid treatment.

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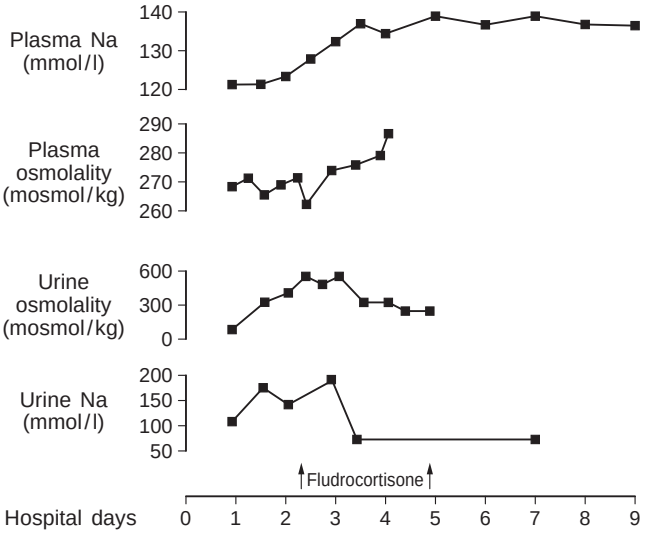
Case report

A 29-month-old black male presented with a 2-month history of weight loss and intermittent fever. A week prior to transfer, he was admitted to a community hospital with diagnosis of atypical pneumonia. Since he developed seizure activity and increased lethargy, he was transferred to Children's Hospital of Louisiana State University Medical Center. On admission, physical examination was remarkable for obtunded mental state. His weight of 12.7 kg was below the 5th percentile. Initial blood pressure was 130/87 mmHg with a body temperature of 38.8° C. His chest X-ray demonstrated innumerable nodes in both lung fields. The findings on magnetic resonance imaging of the brain were consistent with basilary meningitis and communicating hydrocephalus. He was intubated and a ventriculostomy tube was placed. A smear of the endotracheal tube aspirate was positive for acid-fast bacilli and *Mycobaterium tuberculosis* complex RNA was detected. All laboratory results and fluid balance data are depicted in Fig. 1. At the time of admission, his serum sodium was 122 mmol/l, chloride 92 mmol/l, plasma osmolality 269 mOsmol/kg, and urine osmolality 280 mosmol/kg.

By 15 h after admission, urine output had increased to 4.8 ml/kg per hour. Urine sodium was 176 mmol/l, with urine osmolality of 413 mosmol/kg and plasma osmolality of 273 mosmol/kg. His serum sodium was 120 mmol/l. His cortisol and thyroid hormone levels were within normal ranges. ADH level was 7 pg/ml (1.0–13.3 pg/ml, Nichols Institute, San Juan Capistrano, Calif., USA). Aldosterone level was 7.5 ng/dl (reference serum range 9–36 ng/dl, Endocrine Sciences, Calabasas, Calif., USA). Plasma renin activity was 30 ng/dl per hour (supine reference 20–160 ng/dl per hour) and ANP was 400 pg/ml (20–77 pg/ml, Mayo Medical Laboratories, Rochester, Minn., USA).

On the 2nd day of hospitalization, his weight was 11.8 kg. His 24-h urine output was 8,200 ml. Renal ultrasonography showed bilateral hydronephrosis and distended bladder. In addition to a 10-Fr Foley, a 14-Fr suprapubic catheter was placed, and bilateral hydronephrosis resolved. Intravenous albumin infusion and hypertonic saline (3%) were utilized to treat hypotension (82/40 mmHg). Nipride (sodium nitroprusside) and dobutamine were started to maintain blood pressure and peripheral perfusion since the patient was thought to be septic. On day 2, fludrocortisone was initiated at 0.1 mg every 12 h. In the 12 h prior to fludrocortisone, urine output ranged between 300 and 700 ml/h. In the first 12 h after fludrocortisone, urine output never exceeded 100 ml/h. Inotropic support and hypertonic saline were discontinued. His serum sodium normalized in 12 h. Urine osmolality rose to a peak of 564 mosmol/kg and sodium was 189 mmol/l. On the 3rd day of



% 3 NaCl (ml/day)		220	100			
Normal saline (ml/day)	1,528	1,700	763	550	388	
Albumin (ml/day)	260	412	100			
Total intake (ml/day)	2,880	6,324	3,954	4,227	3,313	2,210
Total output (ml/day)	3,347	8,200	3,800	4,291	2,706	1,900

Fig. 1. The clinical course of cerebral salt wasting before and after treatment with fludrocortisone acetate. *Na*, Sodium; NaCl, sodium chloride

hospitalization, fludrocortisone was reduced to 0.05 mg every 12 h and gradually weaned over 4 days. Serum sodium was 139 mmol/l and urine sodium 40 mmol/l. On the 7th of hospitalization, the ANP level was 40 pg/ml.

Discussion

It has become increasingly evident that in pediatric patients with intracranial disorders, such as hemorrhage and infection, hyponatremia can occur in a setting of volume depletion and natriuresis [2–4]. This condition, described as CSW, is completely distinct from SIADH. The wrong diagnosis could lead to inappropriate fluid restriction and worsen the hypovolemia [3]. Therefore, clinicians must be aware of this entity and the clinical features which distinguish CSW from SIADH (Table 1).

As early as 1951, Rapoport et al. [4] described a salt-losing state as a possible cause for hyponatremia in TBM. Up to 1993, however, hyponatremia in TBM was thought to be caused by SIADH [8]. In 1994 Narotam et al. [8] described a state of inappropriate ANP secretion with suppressed or inappropriately normal renin-angiotensin system (RAS) and ADH levels as the cause of hyponatremia in 65% of patients with TBM. ANP can inhibit both renin secretion and angiotensin II-mediated aldosterone secretion in healthy adults on a daily sodium intake of 150 mmol [9]. It has also been reported to suppress the enzymatic activity of renin on angiotensiogen II in dogs [10]. Nawata et al. [11] demonstrated the inhibition of aldosterone biosynthesis by ANP in vitro in cultured human adrenal glomerulosa cells. This hormonal pattern of depressed mineralocorticoid activity and high ANP was present in our patient with TBM. ANP can also effectively inhibit the secretion of ADH. ANP has been reported to inhibit the ADH analogue deamino-D-argino-vasopressin-induced antidiuresis in humans [12]. Samson [13] demonstrated that ANP infusion could significantly reduce plasma ADH levels in rats.

Table 1. Differential diagnosis of cerebral salt wasting (CSW) and syndrome of inappropriate antidiuretic hormone secretion (SIADH)

	CSW	SIADH
Clinical evidence of volume depletion	+	–
Plasma sodium concentration	⇓⇓	⇓
Urine sodium concentration	⇑⇑	Variable
Urine flow rate	⇑⇑	⇓ generally
Net sodium loss	3+	±
Plasma ANP concentration	⇑	⇑
Plasma renin activity	⇓	⇓
Plasma aldosterone concentration	⇓	⇓
Plasma ADH concentration	⇓	⇑

ANP, Atrial natriuretic peptide; ADH, antidiuretic hormone

Aggressive replacement of urine salt and water losses using 0.9 sodium chloride (or 3% sodium chloride if necessary) is the cornerstone of treatment of CSW. It is evident that fluid restriction, which is indicated in SIADH, would be potentially diastrous in CSW. Ishikawa et al. reported the resolution of CSW with fludrocortisone acetate at a dose of 0.2–0.4 mg/day. This treatment was considered because of the associated hormonal pattern of suppressed RAS in CSW [1, 3, 6, 7]. Kappy et al. [3] reported the only pediatric CSW case with subdural bleeding, who responded to fludrocortisone acetate. Our patient demonstrated that mineralocorticoid supplementation could effectively control the natriuresis and excessive urine output secondary to inappropriately secreted ANP in a child with TBM.

It is critical that in any child with hyponatremia and TBM, an evaluation should be undertaken to determine whether CSW or SIADH is present. Excessive natriuresis and hypovolemia should warrant the determination of plasma and urine osmolality, urine and serum sodium, and plasma ANP levels. Mineralocorticoid supplementation seems to be a safe and effective treatment for CSW, whereas normal saline and hypertonic saline could be a temporary measure.

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Literature abstracts

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Response of crescentic Henoch-Schoenlein purpura nephritis to corticosteroid and azathioprine therapy

J. Bergstein, J. Leiser, and S. P. Andreoli

The benefits of treating severe Henoch-Schoenlein Purpura (HSP) glomerulonephritis have not been established. In this study, we evaluate the outcome of 21 children with severe HSP nephritis treated with corticosteroids and azathioprine. Between 1977 and 1995, 78 children (age range 1 to 16 years) were seen for evaluation of HSP. Thirty-one underwent kidney biopsy; indications included nephritic and/or nephrotic onset (15 patients), persistently decreased creatinine clearance (5 patients), or proteinuria >4 g/24 h (11 patients). Twenty treated patients had diffuse mesangial proliferation with crescents in 6–100% (mean 40%) of glomeruli. One treated patient, not biopsied due to extreme obesity, had a creatinine clearance of 49 ml/min/1.73 m^2 and proteinuria of 21.3 g/24 h. These 21 patients were intitially treated with azathioprine and daily oral prednisone (13 patients) or i.v. methyl-prednisolone (8 patients), followed by azathioprine and alternate-day prednisone for 9–24 (mean 15) months. The average follow-up was 32 months. Over the course of follow-up,19 treated patients showed a decline in hematuria (>5 red blood cells/high power field) from 100% to 16% ($P<0.01$), a fall in the serum creatinine from 1.71±2.20 to 0.78±0.25 mg/dl, ($P<0.01$), an increase in creatinine clearance from 76±43 to 122±26 ml/min/1.73 m^2 ($P<0.01$), and a reduction in proteinuria from 8.8±7.5 to 0.47±0.39 g/24 h ($P<0.01$). Two treated patients progressed to end-stage renal failure. There was no difference in outcome comparing patients initially treated with prednisone versus methyl-prednisolone. These observations suggest that corticosteroid and azathioprine therapy is effective in crescentic HSP nephritis.

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Parathyroidectomy after renal transplantation: a retrospective analysis of long-term outcome

T. Schmid, P. Müller, and F. Spelsberg

Background. Advanced hyperparathyroidism refractory to active vitamin D continues to be a problem and frequently forces the nephrologist to resort to parathyroidectomy. One particular aspect is persisting advanced hyperparathyroidism after renal transplantation. Published information on this point is fragmentary.
Design. Retrospective analysis.
Patients. Between 1983 and 1995 a total of 456 patients with renal secondary hyperparathyroidism were subjected to parathyroidectomy (PTX) of whom 103 were transplanted or had at least a history of renal transplantation. The present analysis concerns 37 patients who had a functional renal graft at the time of PTX and were followed for up to 13 years. PTX was performed after an average of 36.7 months after renal transplantation.
Outcome. Thirteen patients experienced rejection and became dialysis-dependent. Twenty-four patients had stable function of the renal graft. Seven patients died during follow-up. Hypoparathyroidism post-PTX developed in 4/37 patients, but could be overcome by replantation of cryoconserved parathyroid tissue.
Frequency estimate. A total of 2632 renal transplants were performed in the catchment area. As a minimum estimate 3.91% of patients with a functional graft required PTX.
Recommendation. Parathyroidectomy should be considered early in cases with advanced secondary renal hyperparathyroidism, since renal transplantation does not necessarily guarantee reversibility of parathyroid overactivity.