Case Report

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Cerebral Salt Wasting Syndrome: A Complication of Meningitis in Hydrocephalus with VP Shunt

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Abstract
Cerebral salt wasting syndrome (CSWS) is an important cause of persistent hyponatremia in children admitted to the intensive care unit. It needs to be promptly differentiated from the syndrome of inappropriate antidiuretic hormone (SIADH) secretion as a cause of hyponatremia in pediatric neurological patients. These two entities often have similar presenting symptoms however the treatment of both can be drastically different, which makes the distinction critical. We present a 6-month-old male child with hydrocephalus secondary to aqueductal stenosis, a blocked VP shunt, meningitis, and hyponatremia. A diagnosis of CSWS was considered and fludrocortisone was started. The patient improved gradually with a reduction in urine output and a gradual increase in serum sodium levels. A diagnosis of CSWS should be strongly considered in hyponatremic pediatric patients with significant natriuresis and suitable treatment should be initiated promptly to prevent long-term neurologic sequelae.

Keywords: CSW; Hyponatremia; Pediatrics; Fludrocortisone; SIADH

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Introduction

Hyponatremia defined as serum sodium < 135meq/l is the single most frequent electrolyte disorder found in sick children admitted to intensive care units. It is commonly seen in critically ill children with traumatic brain injury (TBI) or other cerebral insults secondary to subarachnoid hemorrhage (SAH), subdural hematoma (SDH), epidural hematoma (EDH), aneurysmal clipping or coiling, tumors, or infections (1). Acute hyponatremia may lead to cerebral edema worsening the already pre-existing neurological condition. There are multiple mechanisms associated with hyponatremia in critically ill children, including intravascular volume depletion and hypotonic fluid overload (2).
Once correctable causes of hyponatremia are taken care of, syndrome of inappropriate anti diuretic hormone secretion (SIADH) and cerebral salt wasting syndrome (CSWS) remain the two common differentials.
SIADH was believed to be the most common cause of hyponatremia in the ICU setting but recent studies have shown an incidence of as high as 0.8 to 34.6% for CSWS (3). SIADH needs to be promptly differentiated from CSWS as each has fundamentally different treatment modalities.
CSW is a disorder characterized by ECF depletion and hyponatremia. It causes a true hyponatremia secondary to a cerebral disease causing natriuresis and diuresis (4). The pathophysiology is still not yet understood; however, two mechanisms have been proposed. The first theory is that a direct injury to the central nervous system (CNS) may cause a disruption in the stimulation of the proximal tubules, causing abnormal natriuresis and diuresis (5). The second theory is an increased secretion of

human atrial natriuretic peptide (hANP) and brain natriuretic peptide (BNP) in response to brain injury, results in an increased natriuresis and diuresis (6) .

Evaluation for cerebral salt wasting is done after identification of persistent hyponatremia (serum sodium less than 135 mEq/L) in suspected patients with central nervous system dysfunction. Urine studies are commonly performed to measure urine sodium and osmolality. Urine sodium is typically elevated above 40 mEq/L and urine osmolality is elevated above 100 mosmol/kg.

The patient must also have signs or symptoms of hypovolemia such as hypotension, decreased central venous pressure, lack of skin turgor, and an elevated hematocrit (7).

SIADH has a similar laboratory picture as cerebral salt wasting with hyponatremia and increased urine sodium. However, with SIADH, the patient is euvolemic to hypervolemic from retained free water as compared to the hypovolemic picture of cerebral salt wasting (8). Determination of the fluid volume status has been a key indicator in differentiating between the two. Failure to accurately diagnose these conditions and implement the correct treatment results in an increased mortality risk, a longer length of stay in the hospital, and an increase in the cost of hospitalization (3). Here we report a 6-month-old male child, a case of hydrocephalus secondary to aqueductal stenosis with a blocked VP shunt, meningitis and hyponatremia posing a formidable challenge in determining and treating the cause of hyponatremia.

Case report

A 6-month-old male child, a diagnosed case of hydrocephalus secondary to aqueductal stenosis with ventriculo-peritoneal (VP) shunt insertion surgery performed at 4 months of age, was brought to the emergency department with complaints of lethargy, irritability and food refusal. His mother started noticing an increase in the head size with delayed attainment of milestones postoperatively. There were no focal neurological deficits or seizure episodes prior to admission. On examination, the child was lethargic and drowsy with a weight of 5kg, heart rate of 180 per minute, respiratory rate of 74 breaths per minute, oxygen saturation of 97% on room air, elevated blood pressure of 130/80 mmHg (> 99th percentile), and a head circumference of 47cm with a wide-open anterior fontanel. After admission, the child had multiple episodes of convulsion requiring anticonvulsant therapy (midazolam and valproic acid). Investigations revealed a normal fundus examination and a complete blood count was suggestive of anemia with a hemoglobin concentration of 7.9, hematocrit of 25.9, and total leucocyte count of 15 with a neutrophilic predominance as well as a raised C reactive protein level of 127. Serum electrolytes were suggestive of profound hyponatremia, hyperkaliemia and hypochloremia with a sodium level of 118 mEq/L, potassium level of 5.9 mEq/L, and chloride level of 85 mEq/L (Table 1,2).

Table 1. Lab tests of the patient

Investigations	Result	Normal value
Hemoglobin (g/dl)	7.9	11.1 – 12.6
Corrected Hematocrit (%)	25.9	20 - 24
Leucocyte count (cells per mm^3)	15	6 -17.5
Leucocyte differential	N/L/E/M 55/32/0.8/11	32/61/3/5
Platelets (×103 cells per mm^3)	828	350-550
BUN (mg/dl)	7.3	5-18
Creatinine (mg/dl)	0.3	0.5 – 1.5
Iron studies: Serum iron (mic g/dl) Serum TIBC Serum UIBC	 9.5 258 299	60-180 250 – 450 155 - 300
Ferritin (ng/ml)	100.6	10 - 290
Blood culture	No growth	-
CSF routine Total proteins Total counts (polymorph/leucocyt)	 1347 160 (60/40)	 5.6 – 7.5 0 - 2
CSF culture	No growth	-
Spot urine Sodium (mEq/L)	259	< 40
Spot Urine Creatinine (mEq/L)	10.82	24 - 392
Urine Osmolality (mosm /L)	560	< 100
Serum Osmolality	240	285 - 295
FENa (%)	6.24	< 1

Table 2. Serial sodium levels in the patient

Day of admission	1	2	11	18	19	20	22	23	31	35
Na	118	125	135	115	123	130	129	131	133	135
Urine output (cc/kg/hr)	3	2.5	2.8	5.5	4.6	4	7.4	4.3	3.3	4.7
Fludrocortisone (mg/day)	-	-	-	-	-	0.05	0.05	0.05	0.05	0.05

In view of hyponatremia, isotonic fluid with 0.9% dextrose normal saline (DNS) was started at a maintenance rate calculated using the Holiday-Segar formula. Rapid correction with 3% sodium chloride (NaCl) was not done. Cerebrospinal fluid (CSF) analysis revealed a total count of 15 cells with 80% polymorphonuclear cells and 20% lymphocytes with normal proteins and sugars; therefore, IV antibiotics (cefotaxime and amikacin) were started. Evaluation of persistent hypertension was done. Creatinine (0.3mg/dl), blood urea nitrogen (7.3mg/dl), urine routine microscopy, USG KUB and 2-dimensional echocardiography were all within normal limits. Thus, hypertension was attributed to elevated intracranial pressure and mannitol infusion was started. The child required amlodipine, carvedilol and enalapril for blood pressure control. Computed tomography (CT) of the skull was suggestive of narrowing of the aqueduct of Sylvius with moderate to gross hydrocephalus and bilateral periventricular transependymal CSF seepage suggestive of a blocked VP shunt. VP shunt removal along with reservoir insertion was done on day 7 of admission. After reservoir insertion, routine CSF analysis showed an increase in the total protein (1347) with a raised total cell count of 160 (60% polymorphonuclear cells, 40% lymphocytes) with CSF culture showing no growth. Antibiotics were stepped up to IV ceftazidime. In view of continued hypertension, autonomic dysfunction was considered.

The patient continued to have persistent hyponatremia, despite isotonic fluid administration, and polyuria (> 8cc/kg/day). Further investigation revealed an increase in urine osmolality, urine sodium and urine creatinine (560 mosm/L, 259 meq/L, and 10.82mg/dl, respectively) and a decrease in serum osmolality (240 mosm/L).

Fractional excretion of sodium was elevated (6.24%) (Table 1). As the child's urine output was high with a mildly raised hematocrit, SIADH was ruled out and cerebral salt wasting syndrome was considered. We postulated that there were no signs of dehydration since the patient was on intravenous fluid therapy, which was adjusted for the urine output. Hence, oral fludrocortisone (0.05 mg/day) was started as a treatment modality for cerebral salt wasting syndrome.

Repeat CSF analysis showed a persistently high protein level with a total cell count of 60 (60% polymorphonuclear cells, 35% lymphocytes). Therefore, intrathecal gentamycin was given with alternate day tapping of 25 (5cc/kg) CSF from the reservoir. Gradually, intracranial pressure reduced and blood pressure normalized, so antihypertensive drugs were tapered and discontinued. Investigations showed an increment in the sodium level; thus, fluids were also tapered and omitted. Addition of salt to feeds was done. The urine output decreased markedly in response to fludrocortisone. Repeat CSF on day 31 of admission was suggestive of resolution of infection with a reduction in total proteins (43.8) and total cell count (n=20, 100% lymphocytes); thus, repeat VP shunt insertion was planned on follow-up.

Discussion

Hyponatremia has been reported in 10-50% of critically ill children (9).The common etiologies of hyponatremia include excess fluid therapy, hypotonic fluids, nonosmotic stimulation of ADH due to drugs, pain, and CNS insult. In children with CNS diseases, once the above factors are corrected, cerebral salt wasting and SIADH remain the common differential diagnoses. Both conditions are characterized by hyponatremia with high urinary sodium excretion posing a significant challenge in determining the etiology. As these conditions require different managements, it is vital that an appropriate diagnosis be made (10). SIADH is believed to be responsible for most cases of cerebral disease associated hyponatremia.

Some authors have reported that the prevalence of CSW is almost equal to that of SIADH (10) (Table 2). Cerebral salt wasting syndrome is characterized by hyponatremia, excessive natriuresis, (urine sodium 10 – 20 times normal - usually >140mmol/L), clinical evidence of volume depletion and clinical response to volume and salt replacement, a low serum osmolality with inappropriately high urine osmolality, and polyuria (>5 ml/kg/hour) (7) occurring in patients with central nervous system insults. SIADH is a disease categorized as hypo-osmolar hyponatremia; small amounts of volume expansion are caused by excess renal water reabsorption through inappropriate antidiuretic hormone (ADH) secretion.

There are multiple mechanisms by which intracranial disorders lead to renal salt wasting like impaired sympathetic neural input causing a reduction in proximal sodium and urate re-absorption, impaired release of renin and aldosterone, excessive ANP/BNP secretion or direct neural influence on renal function (10). Our patient had a decreased plasma volume as demonstrated by a high urine-plasma osmolality ratio and a high urine output as well as marked hyponatremia and natriuresis resulting in a negative salt and water balance. In addition, he responded to fludrocortisone (synthetic mineralocorticoid), salt and fluid replacement, thus CSWS was favored over SIADH (Table 3).

Table 3: Differential diagnosis of CSW and SIADH

Factor	CSWS	SIADH
Weight	⇓	⇑
Serum sodium	⇓	⇓
Clinical dehydration	+	-
Water input: Output ratio	<1	variable
BUN	⇑	n
Blood pressure	⇓	n or ⇑
Serum osmolality	⇑ or n	⇓
Urine osmolality	⇑	⇑
Serum uric acid	n	⇓
Urine sodium	⇑⇑	⇑
Urine volume	⇑⇑	⇓ or n
Response to saline infusion	Correct	Temporary and Limited

Mineralocorticoids enhance sodium reabsorption in the kidney by direct action on distal tubule cells, resulting in expansion of extracellular fluid volume. Inappropriate diagnosis may lead to fluid restriction in CSW or fluid and salt supplementation in SIADH. Aggressive treatment is required in CSW but care should be taken not to raise serum sodium > 0.5meq/l/hr as the chance of pontine myelinosis increases with rapid correction (11). A literature review showed successful administration of fludrocortisone in patients with tuberculous meningitis in whom a diagnosis of cerebral salt wasting syndrome was made based on volume depletion and high urinary sodium excretion, which responded to fludrocortisone therapy and subsided. (12). In a series of four cases reported by Taplin et al., fludrocortisone was used for 4–125 days, with doses ranging from 0.2 to 0.4 mg/day. Prolonged and high doses can lead to high blood pressure and sodium and water retention and hypokalemia (13).
A study demonstrated that the use of fractional excretion of uric acid and fractional excretion of

phosphate was not only safe, but also helped to differentiate between SIADH and CSW accurately and consistently (14). Our patient responded to fludrocortisone treatment, which confirmed the diagnosis of cerebral salt wasting.

Conclusion

CSWS has been sparsely described in the pediatric population but it should always be considered as a cause of hyponatremia in cerebral disorders. As treatment, modalities of SIADH are completely different from those used for CSWS, prompt recognition is imperative so that the appropriate treatment can be implemented. In addition to intravenous volume replacement, the use of fludrocortisone is also recommended as an effective treatment for CSWS.

Conflict of Interest

The authors declare no conflicts of interest.

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