CASE REPORT

Cerebral Salt Wasting: A Report of Three Cases

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Abstract

Hyponatremia secondary to the Syndrome of Inappropriate Anti-Diuretic Hormone (SIADH) secretion is commonly observed in patients with various neurological disorders. Cerebral Salt Wasting (CSW) resulting in hyponatremia is also an infrequent occurrence in some patients with neurological disorders. Confusion in differentiating CSW from SIADH may arise since both results in similar electrolyte disturbances. Herein, we report three cases of CSW with intracranial afflictions. CSW was diagnosed on the basis of fractional excretion of urinary sodium and uric acid along with extremely low serum uric acid. Improvements in serum sodium levels after saline hydration and fludrocortisone administration further supported the diagnosis.

Key Words: *Cerebral salt wasting (CSW). Hyponatremia. Fractional excretion. Hydration. Fludrocortisone.*

INTRODUCTION

Hyponatremia is a common disorder that occurs with a number of intracranial afflictions including head injuries, tumors, infections, stroke etc. The Syndrome of Inappropriate Anti-Diuretic Hormone (SIADH) secretion is the cause of hyponatremia in the majority of such cases compared to less frequently reported Cerebral Salt Wasting (CSW).[1-3] Differentiating between SIADH and CSW is challenging at times.[4]

Herein, we report three cases with variable cerebral insults that were subsequently diagnosed with CSW.

CASE REPORT

Case 1: A 25 years old male was admitted with a history of road traffic accident, unconsciousness for 12 hours. His CT scan brain revealed only subcutaneous hematoma at the vertex. Initial vitals and investigations were all normal with a serum sodium (Na) of 138 mmol/l. Five days later his serum sodium was noted to be 126 mmol/L, along with persistent polyuria. Clinical evaluation revealed a Central Venous Pressure (CVP) of 4 cm of water and euvolemic state with high urine output (Table I). Pseudo-hyponatremia was excluded. Serum uric acid was obtained and Fractional Excretion (FE) of uric acid was calculated (Table I). The clinical and biochemical picture of the patient suggested the diagnosis of cerebral salt wasting syndrome. Fludrocortisone 0.3 mg was added on day 11 of admission along with infusions of 0.9% normal saline. Plasma brain type natriuretic peptide (pro-BNP) levels were normal. At day 22 of follow-up, his serum Na was 138 mmol/L and serum uric acid of 5.3 mg/dL (Table I). Fludrocortisone was tapered over the next 3 weeks.

Case 2: A 25 years old male was admitted in ICU with 2 weeks history of vomiting, dizziness, ataxia, headache and altered state of consciousness for one day. He had a GCS of 9/15, bilaterally down-going planters and nuchal rigidity. CT scan of brain was not suggestive of raised intracranial pressure. White blood cell count was raised with predominant neutrophils and serum (Na) of 128 mmol/L. CSF examination was unremarkable. Cannabis addiction was later identified. Clinical evaluation revealed the patient to be hypovolemic when consulted for unexplained polyuria and hyponatremia. His urine output was around seven litres per day with a net negative fluid balance (Table I). In accordance with clinical suspicion he was being treated for meningitis/encephalitis. Pseudo-hyponatremia was excluded and laboratory investigations are shown in table. High Fe of uric acid and the clinical picture of polyuria with volume depleted state suggested the diagnosis of CSW. Fludrocortisone (0.3 mg) was added on day 14 of admission along with 0.9% saline infusions. The polyuria responded and intravenous (IV) fluids were discontinued 2 days later while he maintained his serum sodium. Pro-BNP levels later came out to be normal. The patient was followed after discharge and the urine output and serum Na continued to improve resulting in Na of 138 mmol/L by day 19 (Table I).

Case 3: A 90 years old female was admitted with complaints of left sided weakness for one day. She had a BP of 160/90 mmHg and, systemic examination revealed a GCS of 7 with left sided weakness. Investigations revealed a normal haemoglobin, glucose, creatinine and urine analysis. Baseline serum Na was 132 mmol/L. CT scan of brain showed an infarct in the right middle cerebral artery territory. Nephrologists were consulted when serum Na was 129 mmol/L. She had

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Table I: Patient follow-up.

Patient	Day	S/Na (135 - 150 mmol/L)	S/UA (4.5 - 6 mg/dL)	U/Na	U/Osm	I/O (ml)	FeNa*	FeUA^
1	6	124				3300/3900		
	7	122		108	408	3456/5900		
	11	128	2			5100/5200	1.3%	22.1%
	27	138				2300/2600		
2	1	128				3650/4950		
	3	130				8450/7390		
	9	133				3250/3900		
	13	132	2.1	183	439	2520/3600	4.16%	26.2%
	19	138				2900/2100		
3	1	132				1864/940		
	4	126	2.2	108	408	3920/4430	1.71%	19.82%
	12	130	3.3			4074/3480		25.35%
	18	135				2600/1500		

*Shaded rows indicate the days on which fludrocortisone was started. * Fe Na: Fractional excretion of sodium. ^ Fe UA: Fractional excretion of uric acid.*

Table II: Comparison of CSW and SIADH.

Parameters	Cerebral Salt Wasting	Syndrome of Inappropriate ADH Secretion.
Cerebral injury	Usually evident	May be present
Volume status	Hypovolemic / Dehydrated	Euvolemic / Hypervolemic
Central venous pressure	Decreased	Normal / Increased
Serum sodium	Decreased	Decreased
Urine volume	Increased	Normal / Decreased
Urine osmolality	Increased	Increased
Urinary sodium concentration	Increased	Increased
Fractional excretion of uric acid	High	
Remains high even after correction of sodium.	High	
Brain natriuretic peptide (BNP)	Normal/ Increased	Normal
Treatment	Salt and water repletion along with fludrocortisone.	Salt intake with free water restriction

polyuria and clinically seemed to be dehydrated. Pseudo-hyponatremia was excluded. Intravenous normal saline was started and laboratory investigations are shown in (Table I). Pro-BNP levels were also checked on day 6 which were elevated (159 nmol/L; normal value < 100). The clinical picture and bio-chemical profile was highly suggestive of cerebral salt wasting syndrome. The patient was treated with 0.1 mg of fludrocortisone along with normal saline infusions. The urine output and serum sodium started to improve. Patient had serum sodium of 135 mmol/L on day 18 and was discharged (Table I). Follow-up sodium at one week later was 136 mmol/L. She expired 2 weeks later at home.

DISCUSSION

Hyponatremia secondary to head trauma or other central nervous system pathologies is generally attributed to SIADH.[4] CSW until two decades ago was regarded as a rare entity, although several case reports and case series have been published,[2,3] including a single case report from Pakistan with assumed CSW.[5]

Common to SIADH and CSW is hyponatremia, increased urinary Na excretion and high urinary osmolality, as seen in these patients (Table II). SIADH, however, is a relatively volume expanded state with inappropriately high ADH levels.[4] In contrast, patients with CSW have appropriately high ADH levels secondary to the volume depletion that results from Na loss.[4] This is further complicated by the fact that clinical evaluation of volume status may have its own difficulties as reviewed by Chung *et al*.[6] A net negative fluid balance supports CSW rather than SIADH and may be a clue to the diagnosis, as in these patients.[4] Since we have already published a case of CSW, the diagnosis was considered early on avoiding unnecessary delay due to the misdiagnosis of SIADH.[7] Elevated levels of the natriuretic peptides; ANP and BNP may support CSW, although this may not be a universal finding in all patients.[7,8] In the first two patients, the levels were within the normal range whereas the third patient had an increased BNP level.

Proximal tubular function defects such as decreased Blood Urea Nitrogen (BUN) or serum uric acid in patients with CSW may also help in differentiating it from SIADH.[9] BUN although expected to increase in face of volume contraction may remain normal as in these patients.[4] Increased excretion of uric acid in patients with SIADH is also the result of a defect in net uric acid reabsorption in the proximal tubule.[9] The cause of this defect is unlikely to be volume expansion and remains elusive. The differentiation between SIADH and CSW can, therefore, be made by the observation that Fe uric

acid continues to be high even after correction of hyponatremia in the latter condition.[10] In these patients, the Fe uric acid was higher than 20%.

Management of SIADH and CSW are quite different. Although both conditions require high salt intake, volume restriction is required in SIADH while volume expansion is required in CSW. Wijdicks *et al*. did a retrospective analysis of 134 patients with subarachnoid hemorrhage, of whom 17 patients were diagnosed with SIADH.[2] Condition of 15 of these patients deteriorated after fluid restriction and thus might have had CSW. Management of CSW is fluid replacement with saline and addition of fludrocortisone, similar to the treatment course undertaken for these patients.

Another interesting aspect in these patients was the difference in the initial insult causing salt wasting. In case 1, there was no evidence of actual cerebral injury. Following a detailed literature search, we found two case reports similar to these patients who presented with CSW without evidence of cerebrovascular injury or brain edema.[7]

In conclusion, hyponatremia secondary to CSW in patients with various neurological disorders, even in the absence of obvious injury, is not a rare occurrence. Diagnosis can be established by the presence of volume depletion, low CVP, polyuria, and high fractional excretion of Na and uric acid along with high urine osmolality. Management requires salt and water repletion along with fludrocortisone which needs to be tapered slowly over time.

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