Cerebral Salt Wasting Syndrome in a Patient with Tuberculous Meningitis

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Abstract
We report a case of a 65 year male with meningitis who had polyuria, severe hyponatremia, volume depletion and very high urinary sodium excretion. He was diagnosed to have cerebral salt wasting syndrome based on clinical and laboratory parameters. ©

INTRODUCTION
Hyponatremia is a common finding in hospitalized patients. When hyponatremia is associated with central nervous system disease one would normally think of syndrome of inappropriate ADH secretion (SIADH) as a possibility. We report a case of tuberculous meningitis with severe hyponatremia in whom SIADH was initially considered as the cause and later diagnosed as cerebral salt wasting syndrome (CSWS) based on certain clinical findings and laboratory parameters.

CASE REPORT
A 65 years male who was diagnosed to have tuberculous meningitis based on clinical and CSF findings was started on anti-tuberculosis therapy. Two weeks later he came with history of headache, vomiting and got admitted in the neurosurgical ICU. At the time of admission he was in altered sensorium and the CSF cell count was 755 of which 85% were lymphocytes. The CSF protein was 780 mg/dl and HSV titer was borderline high. Therefore he was started on acyclovir and continued on anti-tuberculosis therapy.

Three days after admission he was found to be dehydrated and his serum sodium was 114 mEq/L and serum creatinine was 3.0 mg/dl. A diagnosis of acute renal failure was made because of severe volume depletion and concomitant acyclovir therapy. He was hydrated well with normal saline and 1.6% saline over the next 2 days. His volume depletion had been corrected with rise of serum sodium to 131meq/L and the serum creatinine decreased to 1.2 mg/dl. His urine output was 1.5 to 2 L/day. Acyclovir therapy was discontinued. The patient was subsequently transferred out of ICU and was followed by the internist. His urine put remained at 1.5 to 2.0 L/day with stable serum creatinine of 1.2 mg/dl during the next 3 days suggesting that he had recovered from the acute renal failure and was not in the polyuric phase of acute renal failure.

He remained stable for the next 3 days after which his urine output progressively increased to 10 L/day and was found to have clinical signs of volume depletion. His lab data revealed serum sodium 120 mEq/L, serum osmolality of 250 mosm/kg, urine osmolality 260 mosm/kg, urine sodium 541 mEq/L, serum creatinine 1.1 mg/dl and serum uric acid 3.1 mg/dl. His 24 hours urinary sodium excretion was 5480 mEq (Normal 40 - 200 mEq/day) and fractional urinary uric acid excretion (FEUA)* was 23.65% (Normal value < 10%). He was started on intravenous saline and received about 15 liters of saline/day for the next many days despite which the serum sodium remained between 120 to 125 mEq/L.

*FEUA calculated by dividing the product of (urinary uric acid (mg/ml) X serum creatinine (mg/ml)) by the product of (serum uric acid (mg/ml) X urine creatinine (mg/ml)) and multiplying the result by 100.

A diagnosis of cerebral salt wasting was made based on clinical findings of severe hypovolemia, very high urinary sodium concentration and excretion, hypouricemia with high fractional uric acid excretion. He was started on fludrocortisone 0.3 mg/day and continued on IV saline for next 3 days. After a week his urine output decreased to 3 - 4 L/day, the serum sodium and osmolality were 130 mEq/L, 270 mosm/kg respectively. His 24 hours urinary sodium excretion decreased to less than 200meq/day. The fludrocortisone dose was reduced to 0.1 mg/day and subsequently stopped after 2 weeks. Four weeks later he came to the out-patient clinic and his serum sodium and
serum osmolality were 135 mEq/l and 280 mosm/kg respectively.

**DISCUSSION**

Hyponatremia is commonly seen in neurosurgical patients especially those with meningitis, encephalitis, brain tumors and intracranial bleeding. Hyponatremia in these patients is often diagnosed and treated as SIADH. Another important condition which mimics SIADH which is often under diagnosed is cerebral salt wasting syndrome (CSWS).

Cerebral salt wasting syndrome is defined as renal loss of sodium during intracranial diseases leading to hyponatremia and decrease in extracellular fluid volume. It can occur between 6 months to 65 years of age and the exact underlying pathophysiology is unclear. One hypothesis is the exaggerated pressure natriuresis in response to increased sympathetic activity and dopamine release. Another postulation is increased release of brain natriuretic peptides and ouabain-like factors by the injured brain.1 Kappy et al1 reported high levels of brain natriuretic peptide and clinical features of cerebral salt wasting syndrome in patients with intra cerebral bleeding and meningitis. Huang et al3 reported cerebral salt wasting syndrome in a 3 year old boy with tuberculous meningitis with hydrocephalus.

Appropriate assessment of volume status would differentiate these two conditions and is the most important clinical finding to differentiate these clinical syndromes. Patients with SIADH would be clinically euovolemic whereas patients with CSWS are always hypovolemic. Invasive monitoring of central venous pressure is more appropriate to assess the volume status especially in those patients who are critically ill. Damaraju et al4 reported that invasive monitoring of central venous pressure and pulmonary capillary wedge pressure is ideal in ICU patients who fulfill the criteria of SIADH and their volume status is inconsistent with diagnosis of SIADH. In such patients a low central venous pressure and pulmonary capillary wedge pressure would suggest cerebral salt wasting syndrome rather than SIADH. Both the conditions are associated with increased urinary sodium excretion and increased release of a natriuretic peptide (Brain natriuretic peptide in CSWS and Atrial natriuretic peptide in SIADH).

Polyuria is common during the recovering phase of acute tubular necrosis. However in this patient the urine output remained around 1.5-2.0 L/day for about 3 days after his renal function stabilized with a serum creatinine of 1.2 mg/dl and the polyuria started later clearly suggesting that it was not the recovering phase of acute tubular necrosis.

Though hypouricemia and high fractional excretion of uric acid (FEUA) is present in both CSWS and SIADH, the FEUA gets normalized in SIADH after the fluid restriction and correction of serum sodium whereas it remains elevated in CSWS.

Differentiation between the SIADH and CSWS is very important because management of these two diseases is exactly opposite. Patients with SIADH require water restriction and increased free water excretion by using loop diuretics, whereas patients with cerebral salt wasting syndrome require volume repletion with saline, high salt intake and fludrocortisone therapy.

We report this patient with tuberculous meningitis in whom the diagnosis of cerebral salt wasting syndrome was made based on severe volume depletion, high urinary sodium concentration and excretion, hypouricemia with high fractional excretion of uric acid and correction of hyponatremia and volume status with saline and fludrocortisone therapy. Eventhough demonstration of elevated BNP levels would support a diagnosis of CSWS, it may not be feasible in every center since the facilities are not commonly available. Though uncommon CSWS needs to be considered in patients with TB meningitis in the right clinical setting.

**REFERENCES**