Case reports

Cerebral Salt Wasting Syndrome: A Case Report

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ABSTRACT

A case of hyponatraemia associated with subarachnoid haemorrhage is presented. The provisional diagnosis of an inappropriate antidiuresis was made and treatment with fluid restriction was instituted. However the patient continued to deteriorate as the diuresis continued and the hyponatraemia worsened, resulting in hypovolaema. The salt wasting syndrome was subsequently diagnosed and saline and fludrocortisone (0.2 mg/day) was initiated, reducing the renal salt loss, increasing the plasma sodium and improving the neurological status of the patient.

Cerebral salt wasting syndrome is an important and under-recognised cause of hyponatraemia in neurosurgical patients, particularly in patients with subarachnoid hemorrhage. It is essential to differentiate it from the syndrome of inappropriate antidiuretic hormone secretion to avoid complications of hypovolaemia and reduced cerebral perfusion as illustrated by this case. Brain natriuretic peptide may be responsible for this syndrome although this requires further investigation. (**Critical Care and Resuscitation 1999; 1: 180-183**)

Key words: Cerebral salt wasting syndrome, subarachnoid haemorrhage, syndrome of inappropriate antidiuretic hormone secretion, hyponatraemia

Hyponatraemia is commonly found in patients with subarachnoid hemorrhage (SAH) as well as in other neurosurgical disorders (e.g. head injury and intracranial infection).[1] In one report hyponatraemia occurred in 30% of cases of SAH. When severe the resulting cerebral oedema exacerbates any pre-existing neurological dysfunction and causes complications that range from confusion and lethargy through to seizures and coma.[2] Iatrogenic water overload, syndrome of inappropriate antidiuretic hormone secretion (SIADH) or a combination of both, have been considered to be the major causative factors.

Peters and colleagues in 1950 reported 3 patients with "a salt wasting syndrome associated with cerebral disease". As their patients responded to salt and fluid replacement, they proposed that the cerebral disease rendered the kidneys unable to conserve salt, leading to sodium and extracellular fluid depletion.[3] While this phenomenon was supported by other studies, identification of SIADH in 1957 by Swartz and Bartter[4] resulted in the cerebral salt wasting syndrome (CSW) becoming a neglected diagnosis. Many authors in fact equated CSW with SIADH. However, recent evidence has accumulated suggesting that many patients with intracranial disease who were initially thought to have had SIADH, were probably misdiagnosed, and had CSW instead.

In patients with SAH, cerebral ischaemia due to vasospasm and hypoperfusion is a major complication, with vasospasm being demonstrated by angiography in up to 60% of patients. The role of maintenance of intravascular volume status and cerebral perfusion pressure in the prevention of sequelae due to vasospasm, and the hypervolaemic augmentation of blood pressure in the treatment of vasospasm is now widely recognised.[5] The detection of CSW (with resultant

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hypovolaemia) is therefore crucial in this setting. Differentiation of CSW from SIADH is also important as the treatment for CSW (i.e. salt and water replacement) is diametrically opposite to the treatment of SIADH (i.e. fluid restriction).

A patient with hyponatraemia caused by CSW, in whom clinical deterioration occurred with fluid restriction, and improvement in neurological status occurred with salt and water replacement, is reported.

CASE REPORT

A 38 year old male was admitted to hospital with a history of acute onset of severe headache, vomiting, ataxia and sudden loss of consciousness. On examination he localised to pain but had no verbal response or eye opening to pain. An endotracheal tube was inserted and mechanical ventilation was initiated. A cerebral CT was performed which revealed a large SAH with extensive intraventricular blood.

Cerebral angiography was performed which showed an anterior communicating artery aneurysm. The patient was transported to the operating theatre and the aneurysm was surgically clipped. His postoperative treatment included intravenous nimodipine 2mg/h. The patient was extubated the next day and was found to be disoriented with a fluctuating level of consciousness. A repeat CT showed reduction in the size of the lateral ventricles with no evidence of hydrocephalus.

As his neurological status progressively improved he was transferred from the Critical Care Unit (CCU) to the high-dependency ward on the 5th postoperative day, with a plasma Na^+ of 138 mmol/L. On the 10th postoperative day the patient became drowsy and disorientated. At this stage the plasma Na^+ was 124 mmol/L, the previous 24 h urine output was 3500 ml with a measured fluid intake of 4000 ml during the same period. The plasma and urinary osmolalities were 262 and 525 mosmol/kg, respectively, and the urinary Na^+ was 173mmol/L (Table 1).

During the next 24 h (i.e. day 11), a diagnosis of SIADH was made and a 1300 ml/day fluid restriction regimen began. However, he became progressively more drowsy and disoriented. The urine volume during day 11 approximated 2 L/24h (with a Na^+ of 115 mmol/L and osmolality 496 mosm/L), and the plasma Na^+ remained at 124 mmol/L. During day 12 with fluid restriction of 500 ml/day, a reduction in plasma Na^+ to 123 mmol/L and further deterioration in the patient's clinical status, the patient was transferred to the CCU. At this stage the patient was difficult to arouse, disoriented in time and place, and could not recognise his family members. A CT scan was performed which was unchanged, showing no evidence of hydrocephalus.

A central line was inserted which revealed an initial central venous pressure of 4 mmHg. In view of a clinical picture of hypovolaemia with evidence of a high urine output, high urinary sodium concentration and high normal value of plasma urea (6.7 mmol/L), the diagnosis of CSW was made. The patient was treated with 1000 ml of 4% albumin in 0.9% saline (Albuminex 4%) followed by 0.9% saline replacement of urinary output. Over 24 h, the plasma sodium increased to 132 mmol/L and the patient became less drowsy.

However, the urinary output continued to be high, varying between 90 to 500 ml per hour. On day 15 the fluid management was changed to a urinary replacement regimen with 0.9% saline minus 80 ml per hour, and fludrocortisone 0.2 mg orally in an attempt to reduce the urinary sodium excretion. This resulted in a fall in urine output (i.e. 2500 ml) and fluid input (i.e. 2000 ml. There was also a reduction in urinary sodium from 85 mmol/L to 57 mmol/L. Plasma sodium increased to 137 mmol/L. The patient continued to improve neurologically and was commenced on an oral diet. Table 1 shows a summary of fluid balance and sodium changes over this period.

Blood samples taken on day 10 and day 12 were processed for renin, aldosterone and cortisol levels. Brain natriuretic peptide and atrial natriuretic peptide[6,7], which have been implicated in CSW, were not measured. Plasma renin activity was 0.38 ηg/ml/h (normal range 1 to 4 ηg/ml/h) and aldosterone was 60 ηg/L (normal range 50 to 300 ηg/L) on day 10 and were lower on day 12 at 0.21 ηg/ml/h and < 25 ηg/L respectively. Plasma basal cortisol level on day 10 was normal (i.e. 420 ηmol/L).

DISCUSSION

Cerebral salt wasting is defined as renal loss of sodium during intracranial disease leading to hyponatraemia and decrease in extracellular fluid volume.[1] Peters *et al*, in 1950 reported three patients with intracranial diseases, hyponatraemia and increased urinary sodium excretion who responded to salt replacement.[3] The authors proposed that reduced secretion of ACTH may have been responsible for suppression of adrenal mineralocorticoid secretion resulting in renal salt wasting. However, Welt *et al* found in their patients with CSW that pituitary-adrenal axis was intact and proposed a defect in direct neural regulation of renal tubular activity.[8] The discovery of SIADH by Schwartz *et al* in 1957 tended to result in all hyponatraemic patients with neurosurgical disorders being labeled as SIADH.[4]

Nelson *et al*, studied hyponatraemia and natriuresis in 9 monkeys with SAH.[9] The natriuresis lasted for 4.5

Table 1. Summary of fluid balance and sodium changes

Post op day	Fluid input /24h (ml)	Urine output /24h (ml)	Plasma Na^+ (mmol/L)	Plasma osmol. (mosm/L)	Plasma urea (mmol/L)	Urine Na^+ (mmol/L)	Urine osmol. (mosm/L)	Na^+ input /24 h (mmols)	Na^+ output /24 h (mmols)	Comments
10	4010	3750	124	262	5.8	173	525	600	680	Drowsy
11	1300	2000 +	124	263	5.8	115	496	150	230 +	Fluid restriction
12	500	1000 +	123	262	6.7	51	569	75	51 +	Patient more drowsy
13	6300	5600	132	271	7.0	85	222	625	467	Fludrocort -isone given
14	6100	5765	137	279	3.9	57	256	350	313	Patient more awake
15	1900	2500	138	277	3.4	38	137	100	95	–
16	2300	2600	136	276	4.2	54	218	100 ++	150	Oral diet

+ = an unmeasured amount greater than the amount documented

days with an average lowest mean sodium level of 125.7 mmol/L occurring on the fifth day. The plasma antidiuretic hormone (ADH) levels were similar to preoperative levels during the natriuresis. Their observations were more consistent with primary natriuresis as a cause of the hyponatraemia than SIADH. The authors speculated that a brain natriuretic peptide may have be responsible for the renal salt loss. Wijdicks *et al*, studied sodium balance and plasma volume in 21 patients with SAH.[10] They found that the plasma volume was reduced in 11 patients and 6 had a negative sodium balance and hyponatraemia. Plasma ADH levels were elevated on admission but declined in the first week regardless of hyponatraemia. They believed that hyponatraemia was due to salt wasting rather than SIADH and should be treated with fluid replacement and not by fluid restriction. The same authors retrospectively studied the relationship between hyponatraemia and cerebral infarction in 134 consecutive patients with aneurysmal SAH.[11] Only 25 of 44 patients with hyponatraemia fulfilled the criteria for SIADH. Twenty-six of the hyponatraemic patients were treated with fluid restriction to correct sodium levels. Cerebral infarction developed in 19 of the 90 patients with normal sodium levels and in 27 of the 44 patients with hyponatraemia ($p < 0.001$). Twenty-one of these were from a fluid restriction group. They concluded that fluid restriction appeared to be dangerous in patients with aneurysmal SAH.

Further support for the concept of CSW has come from a more recent study by Sivakumar *et al* in neurosurgical patients.[12] The main objective of their study was to evolve a management protocol to treat hyponatraemia and natriuresis based on the blood volume status and haematocrit. All 21 patients with hyponatraemia were hypovolaemic including 5 patients with anaemia. They could correct hyponatraemia within 72 hours with isotonic saline (> 50 ml/kg/day) and oral salt (12 g/day) and suggested that most neurosurgical patients with hyponatraemia have hypovolaemia with or without anaemia. They concluded that fluid, salt replacement and blood transfusion rather than fluid restriction often resulted in correction of hyponatraemia.

In another study, Berendes *et al* measured natriuretic peptides, aldosterone, renin, ADH and digoxin-like immunoreactive substances in ten patients with SAH, ten patients with cerebral tumours and 40 healthy controls.[6] All patients with SAH but none of the tumour patients showed an increase in urine output and sodium excretion ($p = 0.018$). The patients with SAH had higher plasma brain natriuretic peptide levels than controls throughout the study period of 7 days. In addition, they had lower than normal aldosterone levels and normal atrial and C-type natriuretic peptides. Their findings strongly suggested that CSW was the major cause of hyponatraemia in aneurysmal SAH, and that the likely cause for this was an increase in brain natriuretic peptide secretion.

Our patient had all the important clinical features of CSW which include hyponatraemia associated with hypovolaemia, high urinary sodium excretion, elevated plasma urea (SIADH is associated with a low plasma urea) and a negative salt balance. Furthermore, there was a beneficial response to saline replacement and

fludrocortisone. Renin and aldosterone levels were significantly reduced in our patient, which may have been secondary to an increased level of brain natriuretic peptide (although these were not measured in our patient). Natriuretic peptides are reported to induce natriuresis through direct tubular effects or by inhibition of renin-angiotensin-aldosterone system.[13]

Management of CSW should be with judicious salt and fluid replacement, colloids to support volume expansion and packed cell transfusion for anaemia. Central venous pressure monitoring may be helpful in patients with hypovolaemia associated with reduced cerebral perfusion. Oral salt and fludrocortisone may also be helpful. Hasan *et al*, in a randomised controlled study, found that oral or intravenous fludrocortisone 0.2 mg twice daily reduced the frequency of a negative sodium balance and natriuresis.[14]

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