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Cerebral Salt Wasting Syndrome in an Elderly Patient with Cerebral Small Vessel Disease

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Abstract

Background: Cerebral salt wasting syndrome is reported in neurosurgical literature from traumatic and non-traumatic brain injuries. No cases have been reported in the medical literature secondary to cerebral small vessel disease.

Introduction: Hyponatremia is a common electrolyte disturbance seen among the acute geriatric admissions with two common diagnostic entities; the secretion of inappropriate antidiuretic hormone (SIADH) and cerebral salt wasting syndrome (CSWS) that have different clinical and biochemical presentations, different pathogenesis and therapeutic approaches.

Hyponatremia caused by CSWS in patients with cerebral small vessel disease (cSVD)- a prevalent condition among the elderly, can be masked in geriatric patients with concomitant fluctuating neurological deficits. Correct diagnosis is crucial to appropriate management.

In this case report we describe an association between hyponatremia caused by CSWS in a patient with cSVD.

Case description: A 79-year-old female with a history of chronic fluctuating confusion and apraxia with declining memory over a year. She presents with another acute fluctuating confusion, apraxia, and moderate hyponatremia detected as an incidental finding. Her biochemistry simulates syndrome of inappropriate antidiuretic hormone secretion. Additionally, her urinary sodium was significantly elevated. Treatment with fluid restriction worsened her hyponatremia but improved on saline infusion. There were no other causes of hyponatremia. Her computer tomography head shows moderate cerebral small vessel disease.

Conclusion: Cerebral salt wasting syndrome is rare in medical admissions as a cause of hyponatremia and remains a diagnosis of exclusion. Cerebral small vessel disease and hyponatremia are common abnormalities among acutely ill geriatric patients. Hyponatremia with significant urinary sodium excretion with a combination of a chronic history of fluctuating neurological deficits with clinical findings and brain imaging suggesting cerebral small vessel disease suggests cSVD as the aetiology of cerebral salt wasting syndrome.

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A combination of chronic history of fluctuating neurological deficits hyponatremia with significant urinary sodium excretion and clinical findings and brain imaging suggesting cerebral small vessel disease can be suggest the aetiology of cerebral salt wasting syndrome.

Keywords: Cerebral small vessel disease, cerebral salt wasting syndrome, syndrome of inappropriate ant diuretic hormone

Introduction:

Hyponatremia is one of the commonest electrolyte abnormalities seen among the acute admissions in clinical practices. It is very common among the elderly patients in acute geriatric medical wards [1,2] and is associated with poor clinical outcomes [3].

The two commonest causes of hyponatremia are the syndrome of inappropriate antidiuretic syndrome (SIADH) and the cerebral salt wasting syndrome (CSWS). It is difficult to differentiate these two conditions clinically and biochemically because of their similarities. The CSWS is defined as hypovolemic hypo-osmolar hyponatremia associated with high renal sodium excretion and urine osmolality [4, 5]. It is very common among those patients who sustain cerebral insults and is well documented among those with aneurysmal cerebral subarachnoid haemorrhages [6,7]. Although, its pathophysiology is not delineated, it is postulated to be due to excess natriuretic peptides secretions from the brain insults [8] and the reduced sympathetic effect on the juxtaglomerular leading to diuresis and natriuresis [3]. The SIADH on the other hand is caused by excessive antidiuretic hormone and presents as euvolemic hypo-osmolar hyponatremia with hypo-osmolar urine and sodium at least between 20-40mOsmol/L. Nevertheless, early differentiation and diagnosis are very important as their treatments differ [9,10].

Although, these conditions are common, no case of CSWS is reported in patients with cerebral small vessel disease (cSVD). We, therefore, describe a case of incidental CSWS in an elderly patient with cSVD presenting with fluctuating neurological deficits.

Case description:

History:

A female in her late seventies who had confusion and declining memory was brought into the emergency department for acute medical admission by her daughter who was concern about her deteriorating conditions. She has had chronic but fluctuating confusion for over a year leading to several prior admissions. She has had no history of head injury, seizure or syncope and her drug history was unremarkable.

Examination:

On this admission, she was noted to be more confused than usual by her daughter and registered an abbreviated mental test score (AMTS) score of 6, although, a formal diagnosis of dementia was not established. AMT is used to identify cognitive impairment in older people but is frequently used for assessing cognition in delirium in all adult patients. The tool on its own does

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not diagnose a person having delirium or dementia, but the result will suggest that cognitive impairment is present, and that further examination is required. She had no other focal neurological deficits but appeared clinically dehydrated with a dry tongue, reduced skin turgor, a blood pressure of 98/55 mmHg with no evidence of sepsis. In the ward, she demonstrated fluctuation of her cognitive function with periods of low and normal AMTS ranging between 6 to 10.

Methods (Differential diagnosis, investigations and treatment)

The fluctuation and the deterioration of chronic confusion associated with apraxia suggested a vascular aetiology. Her blood sugar and all other baseline blood tests were normal except for an isolated moderate hyponatremia of 123mmol/L associated with a calculated serum osmolality of 261mOsmol/L suggesting a hypovolemic hypo-osmolar hyponatremia. This clinically suggested CSWS. However, SIADH was also considered as a differential diagnosis because of its prevalence's in medicine compared with CSWS. Dehydration as a cause of delirium was also considered but the confusion fluctuated despite optimal hydration. Hyponatremia appeared chronic and the level of confusion was clinically perceived as disproportionate.

A casual fluid restriction of ≤ 1L daily was imposed in view of SIADH whilst waiting for her urine osmolality and sodium levels from the laboratory.

A CT head on her second day of admission showed moderate cSVD (Fig. 1) which is known for causing fluctuation in neurological deficits including stepwise deterioration in memory overtime. She complained of inability to walk and felt glued to her chair despite having normal motor functions. Request to get her to stand and walk was not possible, though, she wanted to follow the command. This lasted for several hours and improved in the evening and fluctuated over the next two days of her admission.

Her blood sugar and all others were normal except for an isolated moderate hyponatremia of 123mmol/L with a calculated serum osmolality of 261mOsmol/L suggesting a hypovolemic hypo-osmolar hyponatremia. Provisional diagnosis of delirium secondary to dehydration, hyponatremia secondary to SIADH and vascular dementia were made.

A casual fluid restriction of ≤ 1L daily was imposed in view of SIADH whilst waiting for her urine osmolality and sodium levels from the laboratory.

A CT head on her second day of admission showed moderate cSVD (Fig. 1). She complained of inability to walk and felt glued to her chair despite having normal motor functions. Request to get her to stand and walk was not possible, though, she wanted to follow the command. This lasted for several hours and improved in the evening and fluctuated over the next two days of her admission.

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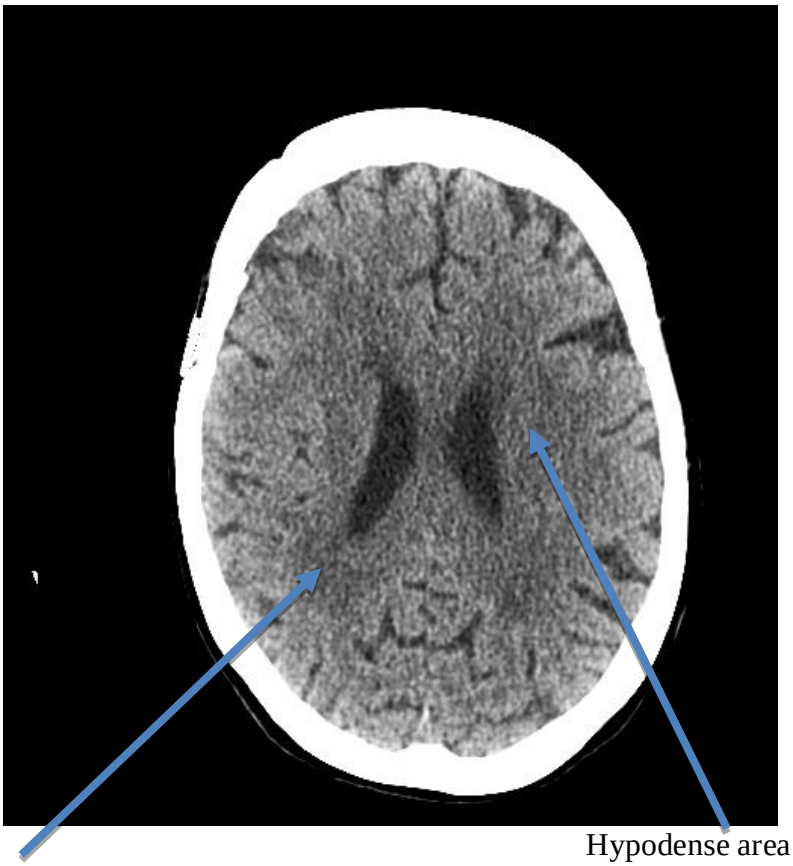

Figure 1: Bilateral periventricular and subcortical low attenuation of white matter changes consistent with moderate cerebral small vessel disease.

Meanwhile, her sodium (122mmol/L) dropped despite fluid restriction. On the third day of admission, her sodium dropped further to 120mmol/L and her serum osmolality was 256mOsmol/L. Her urine osmolality and sodium were 345mOsmol/L and 54mmol/L respectively, suggesting renal sodium loss. Her confusion was objectively better. A revised diagnosis of cSVD complicated by CSWS, apraxia and vascular dementia was made, and she was prescribed 2 L of 0.9% normal saline over 24 hours. After 24 hours of saline infusion, the patient's serum, urinary electrolytes and osmolality (Table 1) continued to improve, and she was discharged on the fifth day after admission.

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Table 1: Cumulative biochemistry and other investigational results

Investigations	**Daily results**						**Reference range (mmol)**
	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 14**	
Serum sodium	123	122	120	123	130	128	**133 - 146**
Serum potassium	5.3	5.2	5.1	5.0	4.9	5	**3.5 – 5.3**
Creatinine	110	100	92	85	80	85	**45 - 84**
eGFR (mL/min/1.73 m²)	44	50	55	56	60	56	**>90**
Serum Osmolality (mOsmol/Kg)	261	260	256	270	276	279	**275 - 295**
Urine Osmolality (mOsmol/Kg)			345			320	**275 - 295**
Urine sodium			54			50	
Serum Uric Acid µmol/L	110				115		**155 - 357**
Thyroid Function Tests	Normal						
Chest X-ray	Normal						
Computer tomography of Head (CT)	Moderate cerebral small vessel disease						

She was seen at the ambulatory clinic a week later with her daughter and has been coping well with usual fluctuations of her confusion without apraxia. She was independent of all activities of daily living but needed support from career twice weekly and her daughter live nearby and provides extra support. Her serum sodium was 128mmol/L, serum osmolality 279mOsmol/L and stable urinary sodium and osmolality. She was discharged from the ambulatory clinic for her GP to follow her up in primary practice. Her progressive sodium over three months remained stable between 26 -31mmol/L.

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Discussion:

CSWS is a common cause of hyponatremia among the neurosurgical patients and is well documented among those with aneurysmal cerebral subarachnoid haemorrhages [6,7]. Although, its pathophysiology is not delineated, it is postulated to be due to excess natriuretic peptides secretions from the brain insults [11] and the reduced sympathetic effect on the juxtaglomerular leading to diuresis and natriuresis [3].

CSWS can occur among the geriatric patients who have high prevalences of both hyponatremia [1] and cSVD [12] after excluding other common causes of hyponatremia. Hyponatremia caused by the CSWS is predominantly hypovolemic hypo-osmolar compared to hyponatremia caused by SIADH where it is euvolemic hypo-osmolar hyponatremia. There is debate as to whether these two conditions are two different entities or the variants of the same condition [13,14]. The former is driven by the natriuretic peptides and the latter by the antidiuretic hormone [10]. They, however, have relatively similar clinical and biochemical parameters and are often difficult to diagnosed early. Nevertheless, it is imperative to make an early differentiation because the treatments vary with fluid administration in CSWS and restriction in SIADH.

Patients with CSWS usually have an history of brain insult, and this could be a pointer towards the diagnosis. However, many geriatric patients, do not have a history of brain injuries but do have undiagnosed underlying cSVD that can present with hyponatremia and other neurological deficits [1,12]. The underlying mechanism causing CSWS in these patients is unknown. However, we postulate that persistent microinfarcts from the cSVD in areas controlling the natriuretic peptide homeostasis leads to excessive secretion as it is seen in those with traumatic brain injuries.

The diagnosis of CSWS can be considered in elderly patients who present with typical clinical and biochemical evidences in the background of lack of potential causes of hyponatremia. Additional evidence can be sought from the presence of the cSVD on brain imaging which often associates with the fluctuation of neurological deficits [15]. This is further supported by the patient's response to intravenous saline infusion rather than restriction.

Several studies [16–18] have recommended certain clinical, biochemical criteria for the diagnosis of CSWS. Some of these tests [17,18] are not readily available in most practices to make a quick diagnosis. We, therefore, propose that an history of fluctuating neurological deficits in the presence of cSVD on brain imaging as supportive parameters for the diagnosis of CSWS in the presence of relevant clinical and biochemical profiles.

Conclusion

CSWS is a rare cause of hyponatremia associated with cSVD. A cluster of clinical signs and symptoms, biochemical parameters and fluctuating neurological deficits associated with evidence of cerebral small vessel disease on brain imaging can clinch the diagnosis. Treatment is with intravenous saline infusion.

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