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# Severe hyponatremia with hypouricemia in a patient with medullary hemorrhage: a case report

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## Abstract

Hyponatremia is the commonest electrolyte abnormality in hospitalized patients and occurs due to various causes. Here we present a case of SIADH who was diagnosed using commonly available biochemical tests. This case report also discusses the interaction of the laboratory physician with the treating clinician and the approach needed to arrive at a correct diagnosis. It highlights the importance of serum uric acid and fractional excretion of urinary uric acid in the diagnosis of SIADH. It also discusses the approach needed to distinguish SIADH from Cerebral Salt wasting syndrome, where the presenting feature is also hyponatremia.

## Key words

Hyponatremia, SIADH, Uric Acid.

## Case Report

A 68 year old gentleman was admitted to the Dept. of Neurology with a history of sudden onset uneasiness followed by slurring of speech and giddiness. Examination by the Consultant Neurologist showed that he was conscious and obeying commands with a Glasgow Coma Scale of 14/15.Power was grade 4/5 in all four limbs and DTRs preserved. After admission MRI of the brain was done and it revealed presence of medullary bleed with perifocal edema. The routine laboratory investigations like complete hemogram, blood glucose, urea, creatinine and serum electrolytes were within normal limits. After initially being treated conservatively, the patient later deteriorated due to aspiration and had to be put on ventilatory support to counter respiratory distress and aspiration pneumonia. While being treated with antibiotics for aspiration pneumonia the patient developed sudden onset severe hyponatremia (109 mmol/L).The patient was treated with 0.9% normal saline but showed no improvement even after 48 hours (112 mmol/L).Serum potassium was within normal range throughout this episode. Due to unavailability of a freezing point osmometer, serum and urine osmolality could not be measured. The Consultant Biochemist suggested spot urine sodium to be done. The urine sodium level was 106 mmol/L. During this time the serum urea level was 4.7 umol/L and uric acid was 71 umol/L. Fractional excretion of uric acid was 18%. Morning serum cortisol was 470 nmol/L and serum TSH was 1.9 uIU/mL. The patient was then put on fluid restriction (500 ml/day) and serum sodium after 24 hours was 123 mmol/L and at 48 hours was 135 mmol/L. At discharge the patient was conscious, oriented, continent and ambulant with one person support. At time of discharge his serum sodium was 139 mmol/L, uric acid 256 umol/L and fractional urate excretion of 4%.

## Discussion

This case has two salient features, first it once again highlights the role of laboratory medicine in arriving at a diagnosis and secondly the importance of prompt therapy after arriving at a provisional diagnosis.
The most common electrolyte abnormality in a hospital population is hyponatremia (1,2). The interesting feature of hyponatremia is that it might present with either hypovolemia, euvolemia and hypervolemia. The first investigation in a case of severe hyponatremia not responding to fluid replacement should be a spot urinary sodium estimation. Urine sodium <20 mmol/L suggests hypovolemia or volume depletion. If urine sodium is >40 mmol/L in a patient with hyponatremia then diuretic use, renal failure, hypothyroidism, hypocortisolism must be excluded before syndrome of inappropriate antidiuretic secretion (SIADH) is considered. Thus serum levels of TSH along with a random serum cortisol was done before a diagnosis of SIADH was made in our patient (3).
SIADH was first described in patients with bronchogenic carcinoma who had elevated levels of antidiuretic hormone without presence of a physiological stimulus. Thus, the level of secretion of the antidiuretic hormone was deemed "inappropriate." Later on researchers found that the antidiuretic hormone in humans was arginine vasopressin. To diagnose SIADH, the urinary osmolality must exceed 100 mOsm/kg of water when the effective plasma osmolality is low. But this approach becomes difficult for institutes who do not have an osmometer, as in our case. But in such a scenario simple biochemical investigations like serum uric acid and urea can be of great help. Hypouricemia, low urea, and a urinary sodium level greater than 40 mmol/L in patients with hyponatremia suggest SIADH (4). Studies show that serum uric acid level of less than 4 mg/dl in cases hyponatremia has a positive predictive value for SIADH of 73 to 100% (5,6). Our experience of SIADH cases diagnosed in our hospital usually have a uric acid of less than 2.5 mg/dl with a concomitant fractional excretion of uric acid if more than 10 %. In our patient persistently low sodium with very high urinary sodium and extremely low level of serum uric acid was due to SIADH. Fractional uric acid excretion (≥10%) is seen in cases of SIADH (7) and in our patient it was 18 %. Fractional excretion of uric acid (FE urate) is calculated using the following formula (urine uric acid × serum creatinine)/(serum uric acid × urine creatinine) × 100. We have also seen some patients with hypocortisolism presenting with hypouricemia and hyponatremia but in such cases FE of urate in urine is not elevated. FE UA can be increased in liver disease like cirrhosis, use of certain drugs like probenecid and after a purine rich diet. In suspected cases of cortisol deficiency if serum basal cortisol shows a borderline normal value our hospital laboratory routinely suggests a short synacthen test before hypocortisolism is ruled out.

After provisionally diagnosing the patient as SIADH we did also consider cerebral salt wasting syndrome (CSWS) as a differential diagnosis, which is also an important cause of hyponatremia particularly in subjects with cerebral hemorrhage. This disorder also presents with hyponatremia, hypouricemia and high fractional excretion of urate. Since both CSWS and SIADH present with similar clinical and laboratory findings, it is difficult to distinguish between them. Yet, it is of utmost importance to distinguish between both as the treatment differs in both of them. The fundamental difference between the two is extracellular fluid (ECF) volume status. Hence CSWS patients are hypovolemic whereas SIADH patients have ECF volume expansion. The pulmonary capillary wedge pressure (PCWP) and central venous pressure(CVP) is high in SIADH while in CSWS it is low. Although it is the best way to differentiate between both, such invasive methods like PCWP and CVP measurement are beyond the scope of routine clinical practice.

The normalization of Fractional Excretion of uric acid after correction of hyponatremia is a key feature which is used to distinguish SIADH from cerebral salt wasting syndrome. In case of CSWS the FE UA is elevated even when the hyponatremia is corrected while in SIADH there is normalization of FE UA (8). The major distinguishing features between SIADH and CSWS is given in Table 1. Conivaptam a vasopressin receptor antagonist is approved by the USFDA for the management if SIADH and has shown good results. This drug promotes electrolyte free water excretion and benefits SIADH. But this therapy should not be used to manage hypovolemic

**Table 1**
Key differentiating features between SIADH and CSWS

| Variable | SIADH | CSWS |
|---|---|---|
| Serum Sodium | Low | Low |
| Serum Uric Acid | Low | Low |
| FE UA | Increased | Increased |
| FE UA after treatment | Reduced | Remains elevated |
| ECF Volume | Increased | Reduced |
| Postural Hypotension | Not Present | Present |
| Central Venous Pressure | Normal | Low |
| Sodium balance | Neutral or slightly raised | Negative |
| Fluid Balance | Neutral or slightly raised | Negative |

hyponatremia like CSWS as it can lead to severe negative water balance (9). With the initiation of prompt therapy by fluid restriction the serum sodium in our patient reached baseline in 48 hours time and so did his serum uric acid. His fractional excretion of urate also decreased thereby suggesting that we were correct in diagnosing this patient as SIADH and not as salt wasting syndrome.
Hyponatremia in a patient might me due to various causes. Biochemical investigations help immensely to arrive at a provisional diagnosis. The diagnosis is of vital importance because the therapeutic action depends on the etiology of hyponatremia be it dehydration, diuretic use, hypocortisolism, hypothyroidism, CSWS or SIADH.

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