CASE REPORT

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Severe hyponatremia due to inappropriate antidiuretic hormone secretion – a case report

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Abstract

Inappropriate antidiuretic hormone secretion syndrome (SIADH) is the most common cause of normovolemic hypotonic hyponatremia in hospital settings. The article describes the case of a female patient admitted to hospital because of life threatening hyponatremia, probably due to SIADH. Laboratory tests and imaging were made to exclude possible causes of inadequate ADH release. 3% saline infusion together with dietary salt supplementation and fluid restriction were applied to restore sodium balance. The patient was successfully treated and discharged home without evident neurological deficits.

Key words

hyponatremia, osmolality, antidiuretic hormone, vaptans

INTRODUCTION

Hyponatremia, defined as serum sodium below 136 mmol/l, is the most common electrolyte abnormality in hospital settings indicating poor outcome, both as the marker for underlying diseases and the disorder itself [1]. The grading of hyponatremia comprises severe, usually symptomatic, hyponatremia with serum sodium below 125 mmol/l, moderate hyponatremia with serum sodium 130-125 mmol/l, and mild hyponatremia with serum sodium 130-135 mmol/l. According to the onset of the disorder, hyponatremia is classified as acute if developed within 48h or chronic if developed within longer time [2].

Differential diagnosis of hyponatremia is based on the evaluation of plasma tonicity, with hypotonic hyponatremia being the most commonly observed abnormality. A further diagnostic step is evaluation of the volume status. This is achieved mostly on physical examination, including blood pressure and heart rate measurement, presence of oedema, dry tongue, and engorged jugular veins. Some laboratory tests, e.g. blood urea, creatinine and urinary sodium excretion, as well as measurement of central venous pressure, are also helpful [3].

Hypovolemic hyponatremia is typical of the renal salt-wasting syndrome, the cerebral salt-wasting syndrome, diuretic excess renal tubular acidosis and Addison's disease, all characterized with urinary sodium above 20 mmol/l. Vomiting, diarrhea or third spacing of fluids may be also responsible for hypovolemic hyponatremia, but they are characterized by urinary sodium below 20 mmol/l. Low serum sodium and hypervolemia is usually observed in cases of renal failure with serum sodium above 20 mmol/l, and heart failure or liver cirrhosis with serum sodium below 20 mmol/l. Normovolemic hyponatremia is mostly the result of SIADH. Some increase in serum sodium may result from both high protein level and hyperlipidemia, a disorder called pseudohyponatremia [4]. Usually underdiagnosed hyponatremia is not properly managed which may result in either cerebral edema with brainstem herniation if left untreated, or demyelination syndrome if corrected too fast [5].

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CASE REPORT

A 50-year-old female patient with a history of left breast cancer – treated with chemotherapy, hormone therapy and radiotherapy, after reconstructive surgery of the left breast within the two preceding weeks – was admitted to the intensive care unit because of extreme weakness (the patient was unable to walk without help), lethargy, confusion, slurred speech, nausea, vomiting and abdominal pain. The symptoms had developed within the preceding few days. On admission, the patient was conscious but responded to pain only. Blood pressure was slightly elevated to 155/95 mmHg, heart rate reached 100/min, and resting ECG was normal. Neither peripheral oedema nor evident pulmonary congestion on auscultation and X-ray were present indicating normal volaemia. There were no evident signs of significant neurological disorders. Brain CT revealed no pathology. Abdominal X-ray and ultrasound were negative for significant diseases (Tab. 1).

The primary diagnosis, derived mostly from the laboratory findings of water and sodium abnormalities, was severe hypotonic normovolemic hyponatremia. To confirm the suspicion of SIADH, which is observed to be the most common cause of such disorders, urine osmolality, urine sodium daily excretion and urine sodium concentration were evaluated and reached the values of 572 mOsm/kg$H_2$0

Table 1. Laboratory characteristics of the patient

Parameter	Value	Reference range
Na	95.5 mmol/l	136-145 mmol/l
K	2.61 mmol/l	3.5-5.1 mmol/l
Ca	1.66 mmol/l	2.15-2.5 mmol/l
P	0.43 mmol/l	0.84-1.45 mmol/l
Cl	55.5 mmol/l	98-108 mmol/l
Protein	5.87 g/dl	6.4-8.3 g/dl
Urea	21.4 mg/dl	11-36 mg/dl
Uric acid	2.4 mg/dl	2.4-5.7 mg/dl
Serum osmolality	235.6 mmol/kg H_20	270-300 mmol/kg H_20
Cortisol 8:00 a.m.	163.6 ng/ml	62-194 ng/ml
Cortisol 8:00 p.m.	252.9 ng/ml	23-119 ng/ml
ACTH	10.76 pg/ml	7.2-63.6 pg/ml
TSH	0.356 µlU/ml	0.27-4.2 µlU/ml
TG	55 mg/dl	150-200 mg/dl
Glucose	97.5 mg/dl	60-100 mg/dl
Creatinine	0.5 mg/dl	0.6-1,1 mg/dl
Urine osmolality	572 mOsm/kg H_20	300-900 mOsm/kg H_20
Urine sodium	93 mmol/l	54-190 mmol/l

(reference range 300-900 mOsm/kg H_20), 434 mmol/24h (reference range 40-220 mmol/24h) and 93 mmol/l (reference range 54-190 mmol/l), respectively. Based on these results, SIADH was diagnosed. Chest CT, abdominal MR and left breast MR were made to identify possible source of ADH, including tumours and infiltrations, especially of neoplastic origin. Brain MR was also performed both to exclude possible cause of SIADH, as well as to check for any organic brain disease resulting either from hyponatremia or rate of sodium correction if too fast.

Results of all imaging did not reveal any evident cause of SIADH. The patient used to be treated both with chemotherapy and antidepressive drug tianeptine but none of them was proved to induce SIADH. Moreover, this treatment had been applied much earlier, before the onset of the present disorder which was acute in onset.

According to the medical records which the patient brought with her, two days before admission to our hospital the patient's serum sodium was within normal range. For the first two days of hospital stay the patient was treated with 3% saline infusion and fluid restriction. Serum sodium was measured every several hours and within 24 hours its concentration increased from 95.5 mmol/l to 110 mmol/l. Other electrolytes were also corrected. The rate of sodium correction was decreased gradually and the patient was switched to diet the rich in salt (Tab. 2). Fluid restricted to 800-1,000 ml a day was continued. Loop diuretic furosemid was added at the daily dose of 20 mg.

After three weeks of hospital stay the patient was discharged home stable, ambulant, serum sodium about 133 mmol/l, and without significant persistent neurological deficits.

DISCUSSION

SIADH is the most common cause of hypotonic normovolemic hyponatremia [6, 7]. The first step in diagnosing

Table 2. Serum sodium correction rate

Date	Na (mmol/l) value
10.05.2012	95.5
10.05.2012	99
10.05.2012	96
11.05.2012	104
11.05.2012	110
12.05.2012	118
12.05.2012	121
13.05.2012	122
14.05.2012	123
15.05.2012	120.9
16.05.2012	119.0
17.05.2012	114.7
17.05.2012	115.0
18.05.2012	112.0
19.05.2012	118.0
20.05.2012	118.0
21.05.2012	120.0
22.05.2012	119.0
23.05.2012	123.0
24.05.2012	128.0
25.05.2012	123.0
26.05.2012	127.0
28.05.2012	132.0
29.05.2012	133.0
30.05.2012	132.8

SIADH is to exclude other disorders resulting in similar water and sodium abnormalities, including hypothyroidism, glucocorticoid deficiency and excessive intake of hypotonic fluids [3]. The patient seemed normovolemic, with normal TSH as well as glucocorticoid, protein and lipid status, therefore SIADH was suspected, and attempts were made to confirm the primary diagnosis. The approved criteria to diagnose SIADH are listed below [6, 7].

DIAGNOSTIC CRITERIA FOR SIADH:

- serum osmolality < 275 mOsm/kg H_20;
- urinary osmolality > 100 mOsm/kg H_20;
- normovolemic status;
- urinary sodium > 40 mmol/L;
- normal function of thyroid and adrenal glands;
- no use of diuretics (one week before evaluation);
- serum uric acid < 4 mg/dl;
- blood urea nitrogen < 10 mg/dL;
- improvement with fluid restriction.

All the above criteria could not be fulfilled, but most of them, including urine osmolality, urinary sodium excretion, urinary sodium concentration, serum uric acid, were found in the patient. Urinary sodium greater than 40 mmol/l is especially typical of SIADH [8, 9]. It was also not possible to obtain vasopressin concentration in the plasma, but it must be mentioned that its level also exceeds normal values in other than SIADH-induced cases of hyponatremia [10, 11].

Neither laboratory tests nor imaging revealed any obvious cause of SIADH, the most common of which are listed in Table 3 [8, 9]. Vasopressin may be released from the hypothalamus in response to any stress, including pain, nausea, fear, trauma and mental disorders. A genetic origin of SIADH has been also described, including the nephrogenic and hypothalamic types. Some cases of SIADH are finally diagnosed as idiopathic [8, 9]. The cerebral salt-wasting syndrome mostly observed after brain injury due to trauma or neurosurgery, may be mistaken for SIADH since its biochemical profile is similar. The most important difference is hypervolaemia in the cerebral salt-wasting syndrome, compared to normovolemia in SIADH, as well as treatment with fluid supplementation in one and fluid restriction in the other [4].

Table 3. Identifiable causes of SIADH

Neoplasms: lung cancer, pancreatic cancer, leukemia, sarcoma
Neurological disorders: meningitis, encephalitis, brain tumour, subarachnoid haemorrhage
Lung diseases: pneumonia, bronchial asthma
Endocrine disorders: hypothyroidism, glucocorticoid deficiency
Drugs: selective serotonin reuptake inhibitors, tricyclic antidepressants, thiazides, vincristine, cisplatin

According to the time onset and severity criteria, the patient was diagnosed with acute severe hyponatremia with need of urgent correction. The recommended management is with 3% hypertonic saline infusion with serum sodium measurements every 2 to 4 hours within the first 24 h. The goal is to correct sodium concentration to 120 mmol/but no more than by 20 mmol/l within the first 24 hours. Consecutive sodium measurement confirmed the suggested correction rate. Left untreated, hyponatremia may be life threatening with brain oedema, herniantion, and sudden death being the most dangerous complications. Too fast correction of serum sodium may lead to demyelination syndrome [2]. Fluid restriction to 500-1,000 ml a day is also suggested in the treatment of SIADH-related hyponatremia. If difficult to accept by the patient it can be less rigorous in combination with loop diuretics. Recommended daily sodium intake should be about 9 g [2, 5]. Arginine vasopressin antagonists vaptans blocking V2 receptors seem to be effective in the treatment of SIADH, and both tolvaptan and conivaptan have been approved by relevant committees. This therapy increases thirst, but most importantly, its high cost makes it unavailable in everyday practice [12, 13]. Demeclocycline, lithium, phenytoin and urea are no longer used in the treatment of SIADH, being mentioned in literature only for historical reasons [5].

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