Case Report

The dilemma of diagnosing the cause of hypernatraemia: drinking habits vs diabetes insipidus

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Introduction

Fortunately, hypernatraemia is not a common problem, occurring in <1% of patients in an acute care hospital. It is serious, however, as hypernatraemia is correlated with a high mortality rate [1]. A major reason that hypernatraemia is so rare in conscious adults is the presence of powerful, highly regulated responses to a rise in plasma osmolality, namely thirst and anti-diuretic hormone (ADH) release [1]. An increase in plasma osmolality of only 2 mOsm/kg above normal values stimulates thirst and ADH release, and ADH in turn causes water reabsorption by the kidney. Since osmolality is determined by the ratio of osmotically active particles to the volume of water in the body, thirst plus ADH release act to increase the volume of water in the body and correct the tendency to develop hyperosmolality/hypernatraemia. Clearly, both thirst and ADH release are required because failure to release ADH or failure of ADH to stimulate water reabsorption by the kidney does not increase the osmolality or plasma sodium concentration as long as the subject has access to water [1]. Therefore, hypernatraemia in a conscious patient implies that there is a defect in thirst mechanisms in addition to loss of water via the kidney, gastrointestinal tract or other routes.

We encountered a previously healthy young man who developed hypernatraemia (serum sodium concentration, 169 mEq/l), but did not complain of thirst. Following correction of the hypernatraemia, we investigated him for disorders that could limit ADH responses as well as thirst. He was found to have a degree of partial central diabetes insipidus, but psychotic depression interfering with thirst mechanisms was the major factor accounting for hypernatraemia. With proper treatment, the hypernatraemia was reversed and has not recurred.

Case

The patient is a 19-year-old man who had been incarcerated for 4 months. His mother reported that before he was jailed, he had played on the high school basketball team, weighed close to 200 lb and was healthy. During his incarceration, he was noted to be eating poorly, becoming more dishevelled and appeared to be losing weight. He was found to have hypernatraemia and was sent to our Emergency Room. Upon arrival, he was in shock (blood pressure 80/40 mmHg, heart rate 136/min, plus mental confusion) and was immediately given 1 l of Ringer’s lactate solution and 1 l of normal saline. The hypotension resolved and urine was collected to measure sodium, chloride and osmolality. After these infusions, he became oriented to person, place and time, but remained dishevelled and had a somewhat flat affect. Despite repeated questioning and urging, he denied being thirsty or having been thirsty over the prior 4 months. There were no focal neurological abnormalities and the only physical abnormality was a generalized decrease in strength.

Initial values of serum chemistries are shown in Table 1. Values of urine sodium and chloride concentrations obtained after he had received intravenous Ringer’s lactate and normal saline were 77 and 79 mEq/l, respectively; urine osmolality was 1121 mOsm/kg. There was a low anion gap and no metabolic acidosis. The low anion gap was possibly related to a low serum albumin (3.3 g/dl) that was not attributable to proteinuria, and drug screen was negative. Computed tomography (CT) of the skull revealed no evidence of trauma or other abnormalities.

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Table 1. Summary of laboratory results

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>After treatment</th>
<th>Water deprivation (max)</th>
<th>3% saline challenge (max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Na (mEq/l)</td>
<td>169</td>
<td>144</td>
<td>145</td>
<td>151</td>
</tr>
<tr>
<td>S K (mEq/l)</td>
<td>4.2</td>
<td>4.5</td>
<td>4.5</td>
<td>4.2</td>
</tr>
<tr>
<td>S Cl (mEq/l)</td>
<td>133</td>
<td>107</td>
<td>108</td>
<td>118</td>
</tr>
<tr>
<td>S CO₂ (mEq/l)</td>
<td>31</td>
<td>28</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>S BUN (mg/dl)</td>
<td>84</td>
<td>10</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>S Cr (mg/dl)</td>
<td>1.7</td>
<td>0.87</td>
<td>0.93</td>
<td>0.98</td>
</tr>
<tr>
<td>S Osm (mOsM/kg)</td>
<td>398</td>
<td>292</td>
<td>303</td>
<td>308</td>
</tr>
<tr>
<td>U Osm (mOsM/kg)</td>
<td>1128</td>
<td>262</td>
<td>786</td>
<td>–</td>
</tr>
<tr>
<td>P AVP (pg/ml)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>5.01</td>
</tr>
</tbody>
</table>

To treat the hyperosmolality, we urged him to drink, but this proved to be unsuccessful as he expressed no desire to do so. We placed a nasogastric tube and infused water at a rate of 1 1 every 4 h. Twelve hours later, his serum sodium was 158 mEq/l but he still denied being thirsty. His serum sodium was corrected to normal values by this therapy and his body weight increased by 6 kg, however he still had no desire to drink nor did he note that he had been thirsty earlier.

To evaluate potential causes of hypernatraemia, pituitary function was evaluated by measuring serum levels of follicle-stimulating hormone, luteinizing hormone, thyroid-stimulating hormone, free thyroxin, and cortisol. All values were within normal limits. To search for a structural abnormality in the hypothalamic–pituitary region, a magnetic resonance imaging (MRI) scan was obtained 3 days after admission, and revealed nodularity of the infundibulum and tuber cinereum; these abnormalities were interpreted as evidence for inflammation. In addition, there were no hyperintense signals present in the posterior pituitary, suggesting that ADH was absent [2]. The problem was complex, however, because the patient had no thirst with severe hyperosmolality. Since there are cases of hypodipsia related to psychiatric abnormalities, we obtained a psychiatric consultation which found elements of depressive psychosis, and therapy with sertraline and haloperidol was begun. Subsequently, he was discharged to a mental health facility with detailed instructions to monitor body weight, blood pressure and serum sodium.

Because of the radiological abnormalities in the pituitary, we arranged for a water deprivation test 10 weeks after his initial admission. After 4 h of water deprivation, serum sodium and plasma osmolality increased (Table 1) and urine osmolality was 786 mOsM/kg while serum ADH values measured by the clinical laboratory were zero. These values do not exclude partial central diabetes insipidus and we were concerned about the reliability of the plasma ADH measurement; in addition, he had been taking psychiatric medicines [3]. Consequently, we readmitted the patient 2 weeks after withholding psychiatric medications (~24 weeks after the initial admission). No other episodes of hypernatraemia had occurred and there was evidence of improved interactions with the staff, and his diet consisted of normal amounts of protein and salt, resulting in a weight gain of almost 40 lb. Upon questioning, he noted that shortly after his incarceration he had become depressed and even heard voices telling him not to eat or drink; these problems had not reappeared after his initial hospitalization. A second examination of the sella turcica by MRI revealed persistent mild thickening of the pituitary stalk, interpreted as possible inflammation and, again, there was absence of the hyperintense signal in the posterior pituitary compatible with an absence of ADH. To determine whether there was partial central diabetes insipidus, a second water deprivation test was performed. After an overnight fast and 7 h without water, the maximum urine osmolality was 666 mOsM/kg but the sodium did not rise above 143 mEq/l and, hence, the test did not meet the rigorous criteria for abnormal ADH responses (i.e. Na > 145 mEq/l or osmolality > 300 mOsM/kg). At this sodium concentration, the plasma vasopressin (AVP) concentration measured by D.G.B. was 2.22 pg/ml (normal = 1–5 pg/ml with normal serum sodium values) [1,4]. Subsequently, he received an infusion of hypertonic saline and the serum sodium and osmolality increased (Table 1); plasma AVP increased to 5.01 pg/ml. The patient did note some degree of thirst during the test. We interpreted these values as being consistent with partial central diabetes insipidus, but concluded that the principal problem that had caused hyperosmolality was absence of normal thirst mechanisms.

Discussion

What caused the profound hypernatraemia leading to hypotensive shock in this previously healthy young man? Because thirst is such a powerful response to hyperosmolality, we initially thought there could be a hypothalamic lesion interfering with both thirst and ADH release [1,5]. Traditionally, the threshold for becoming thirsty is a plasma osmolality of 290 mOsM/kg and, above this value, the sensation of thirst increases rapidly, becoming very intense at plasma osmolality values > 300 mOsM/kg [6]. Extensive radiographic examination and measurements of anterior pituitary hormones did not uncover a hypothalamic lesion. Although hypodipsia is generally associated with an abnormality around the hypothalamus, other areas of the central nervous system (CNS) can be involved [1,5]. Miller et al. found defective thirst in six geriatric patients who had non-hypothalamic CNS disorders following prior cardiovascular accidents [7]. The patient we describe had no detectable CNS structural lesions and there was no persistent abnormality in water metabolism after treatment of his psychiatric abnormalities. Consequently, we do not believe his hypernatraemia was caused by a structural defect in the hypothalamus.

A second possibility is that diabetes insipidus was the principal abnormality causing hypernatraemia...
in this patient. This is unlikely because, upon admission, the patient had concentrated urine, but we do not believe this excludes a degree of diabetes insipidus because he was severely hypotensive. As noted by Valtin and Edwards, a low glomerular filtration rate results in a very low volume of urine and a markedly concentrated urine sodium; it is also possible that there was some release of ADH that acted to concentrate the urine [8]. During the second water deprivation test, the urine did concentrate, but not above 666 mOsm/kg (values as high as 900 mOsm/kg have been observed with partial central diabetes insipidus) [1]. Notably, his intake of protein and salt were normal so the medullary interstitium should not have been impaired by a poor diet. Furthermore, we found that the plasma ADH level during hypertonic saline infusion rose only to 5.1 pg/ml and, hence, would be characterized as a minimal response to hyperosmolality [1]. Finally, the MRI examination did not show hyperintense signals in the pituitary that are present with normal vasopressin stores. We interpret these results as indicating that the patient has a limited vasopressin reserve and, hence, partial central diabetes insipidus. We do not believe the patient had an abnormal resetting of his osmolality regulatory centre because his serum sodium and osmolality became normal after hypernatraemia was corrected, even when psychiatric drugs were withdrawn [1,5].

A third possibility is that psychiatric abnormalities led to the perception that he was not thirsty. Impaired drinking is suggested because hypernatraemia is unusual with diabetes insipidus alone unless there is impairment in the ability to drink. Likewise, abnormal drinking behaviour alone is an unusual cause of hyperosmolality unless the subject is unable to conserve water because of kidney losses (e.g. during an osmotic diuresis), or losses through the gastrointestinal tract or via perspiration. It was interesting that the patient had improvement in his sensation of being thirsty after he received anti-psychotic medications. Grouping of psychiatric and physiological abnormalities is distinctly unusual; hypodipsia has been reported as an acquired cause of hypernatraemia in only a few instances [9–11]. In those reports, only one group evaluated the hypernatraemic patient for defective water metabolism and they concluded that the patient had no evidence of diabetes insipidus [9]. In short, an inadequate fluid intake causing hyperosmolality is distinctly abnormal because thirst is one of the most powerful behavioural drives experienced by humans [5,6]. Thus, the absence of thirst undoubtedly played a major role, but the concomitant abnormality in ADH release contributed to the development of hypernatraemia.

We do not believe that his disorder was due to even more unusual lesions such as an occult germinoma, as has been reported in children who were found to have isolated diabetes insipidus and thickening of the pituitary stalk. The normal values of anterior pituitary function and a normal β-human chorionic gonadotrophin provide evidence against this diagnosis. Other causes of thickening of the pituitary stalk include neurosarcoidosis, Langerhan’s histiocytosis, lymphocytic hypophysitis and disorders of unknown origin [1]. Since he has recovered the sensation of thirst and there have been no further episodes of hypernatraemia, the major abnormality appears to have been psychiatric in origin.

In summary, hypodipsia–adipsia from psychiatric disturbances can occur and is potentially reversible. The influence of ADH on water metabolism is so strong, however, that the presence of severe hypernatraemia should prompt an evaluation for defects in ADH secretion or its action. Regaining normal drinking behaviour following psychiatric disorders can take weeks or even months, but appropriate therapy can prevent further episodes of hypernatraemia.

Conflict of interest statement. None declared.

References


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