Hypernatremic Hydrophobic Transient Adipsia Without Organic or Severe Psychiatric Disorder

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Context: Psychogenic adipsic hypernatremia is an exceedingly rare and life-threatening condition, occurring in those with severe psychiatric disorders. Its diagnosis requires exclusion of congenital or acquired hypothalamic pathologic entities. We present the case of a patient who experienced transient severe hypernatremia without evidence of brain pathologic features or known psychiatric disease. In our patient, the transient adipsic hypernatremia had resulted from an episode of mild depression that resolved spontaneously.

Case Description: A 46-year-old healthy woman who had had three recurrent admissions within 1 month had presented for evaluation of intractable nausea and vomiting with a history of a recent episode of a depressive mood change. Each admission had shown substantial hypernatremia (maximum plasma sodium, 166 mEq/L) accompanied by a strong aversion to consuming water. The findings from the diagnostic evaluation showed elevated serum osmolality and lower than expected urine osmolality (urine osmolality range, 474–501 mOsm/kg). This finding, along with an MRI scan showing the presence of a normal posterior pituitary bright spot, suggested that the osmoregulation of her thirst and arginine vasopressin (AVP) secretion were both defective during the attack. The patient was evaluated by psychiatry. Mild depression was diagnosed, and the patient started treatment with mirtazapine, which she only took for a few days. The patient's hypernatremia had completely recovered with resolution of her depression within 2 months.

Conclusion: A mild mood disorder can cause transient dysregulation of the thirst mechanism and AVP secretion through not yet identified mechanisms. **(*J Clin Endocrinol Metab* 104: 5427–5430, 2019)**

Adipsic hypernatremia is a rare, life-threatening disorder in which the total body water becomes abnormally decreased owing to a defect in osmotically stimulated thirst and water intake. In many patients, adipsia will be associated with a congenital or acquired hypothalamic pathologic lesion, which permanently impairs the osmoregulation of thirst and the secretion of the antidiuretic hormone, arginine vasopressin (AVP) (1). Despite the severe defect in the osmoregulation of AVP, the response to nonosmotic stimuli will be normal and overt defects in urine concentration will be uncommon, indicating that the posterior pituitary is intact. In others, however, the defect in thirst will not be associated with demonstrable pathologic lesions in the hypothalamus or a defect in the osmoregulation of AVP secretion (2–4). In two patients, as well as several others in whom the osmoregulation of AVP secretion had not been evaluated directly (5, 6), the adipsia and hypernatremia appeared to be episodic and associated with severe psychosis. Urine osmolality tended to be high during the episodes and, in one patient (5), a follow-up MRI revealed the absence of the normal posterior pituitary bright spot.

Abbreviation: AVP, arginine vasopressin.

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In the present report, we have described the case of a relatively healthy patient without demonstrable brain pathologic features or any important psychiatric history who was admitted to a general medicine ward three times within 1 month because of substantial hypernatremia. During these episodes, she expressed a strong aversion to consuming water and other fluids but not to consuming food. The diagnostic evaluation revealed the presence of a normal posterior bright spot on the MRI scan and was otherwise negative except for a psychiatric diagnosis of mild depression for which she was treated with mirtazapine for a few days. She recovered completely, and during a 6-month follow-up period she maintained her serum sodium within the normal range. To the best of our knowledge, ours is the first reported case of transient hypernatremic hydrophobic psychogenic adipsia without major organic or psychiatric pathologic features.

Case Report

Our patient was a 46-year-old woman who had had three recurrent admissions within 1 month for evaluation of intractable nausea and reported vomiting. The patient had reported nausea and vomiting associated with liquids but not solid food and unintentional weight loss of 15 lb. She had denied abdominal pain, diarrhea, polydipsia, and polyuria and had reported decreased urinary output for 1 week with urine that was concentrated. Her husband reported that she had seemed depressed as of late and that she had had a similar presentation 7 years before this episode, which had been associated with a depressive mood. She had undergone an extensive evaluation at that time that was nonrevealing. During the third admission, on examination during an endocrine consultation, the patient had a body mass index of 28.9 kg/m^2, blood pressure of 119/68 mm Hg, heart rate of 109 bpm. She was alert and oriented, with normal neurologic examination findings but was noted to have a very flat affect. The laboratory evaluation at the third admission revealed a maximum plasma sodium of 166 mEq/L (normal range, 135 to 145 mEq/L), potassium of 4.5 mEq/L (normal range, 3.5 to 05.0 mEq/L), chloride of 121 mEq/L (normal range, 100 to 110 mEq/L), bicarbonate of 20 mEq/L, urea nitrogen of 26 mg/dL (normal range, 8 to 20 mg/dL), creatinine of 2.3 mg/dL (normal range, 0.6-1.4 mg/dL) serum osmolality of 345 mOsm/kg (normal range, 270 to 300 mOsm/kg), and urine osmolality of 474 mOsm/kg (normal range, 50 to 600 mOsm/kg). The values from urine osmolality were obtained after the patient had received 3 L of normal saline 0.9% on admission, with continued dextrose 5% in water. The thyroid function test results and plasma cortisol levels were normal. The administration of intravenous fluids had been the mainstay of therapy during the three recurrent admissions, and patient had been discharged each time once her sodium levels had normalized. More information about the three admissions are presented in Table 1 and Fig. 1. During these three hospital presentations, the patient had undergone extensive evaluations, including esophagogastroduodenoscopy and a gastric emptying study, with normal findings. An MRI scan of her brain noted the bright signal spot of the posterior lobe of the pituitary gland (Fig. 2). Observed during several visitations by the endocrine service was her marked aversion to drinking water or any other fluids. When the patient was handed a glass of water, she would refused to drink and, with continued encouragement, would only take a small sip of water, which she immediately expelled. She denied any thirst and also denied any nausea and disgust specifically related to drinking water. Assessed by psychiatry as being depressed, she was treated with mirtazapine 7.5 mg daily. After this treatment, the patient had become slightly more disposed to drinking fluids. She improved clinically, and at the time of discharge, her plasma sodium had corrected to 144 mEq/L. Eight weeks later, her plasma sodium remained at 144 mEq/L with a normal serum osmolality of 298 mOsm/kg. At 16 weeks after her last admission, the patient's flat affect had disappeared completely, and she was not taking any psychoactive medications. Also, she reported that she had discontinued the mirtazapine shortly after her discharge during the last admission, and she had a normal serum sodium level of 138 mEq/L. During this encounter with the patient, although she did

Table 1. Laboratory Data at Admission for the Three Hospital Medical Admissions

Admission No.	Plasma Sodium, mEq/L (135–145)	Plasma Potassium, mEq/L (3.5-5)	Urea Nitrogen, mg/dL (8–20)	Plasma Osmolality, mOsm/kg (270–300)	Urine Osmolality, mOsm/kg (50–600)	Urine Electrolytes	Plasma Sodium at Discharge, mEq/L
3	163	4.5	26	345	474		144
2	158	4.6	30	338	501		138
1	154	4.1	26	—	523	Na <10 mEq/L; Cl <15 mEq/L; K, 33 mEq/L	142

Normal levels in parentheses.

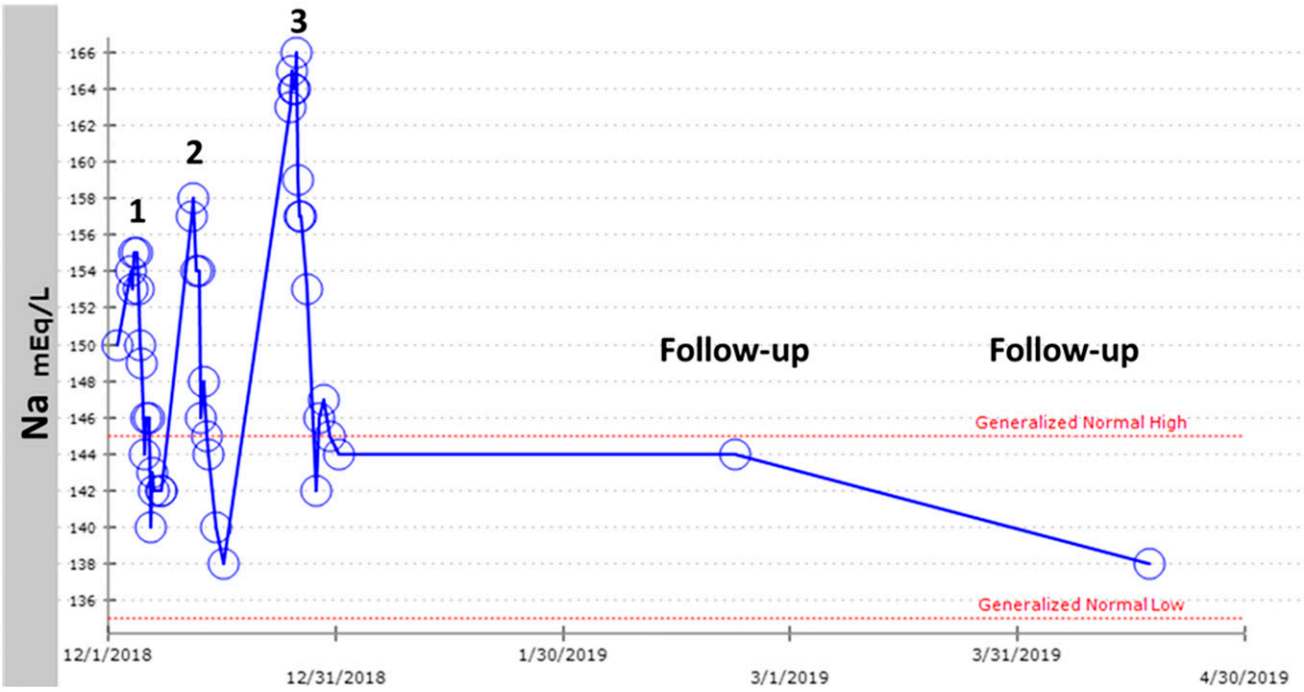

Figure 1. Plasma sodium levels during the three hospital medicine admissions (labeled 1, 2, and 3), including the high levels at admission and the decreasing levels after fluid administration. The sodium levels had normalized at the two follow-up visits.

not report thirst, she did consume water when requested without aversion.

Discussion

The case of the present patient is unique, to the best of our knowledge, in that she presented with severe transient hypernatremia with adipsia and hydrophobia without an organic disease or severe psychiatric background. Adipsia and hydrophobia had been diagnosed at the bedside simply by observing that the patient denied thirst and avoided drinking spontaneously. The patient had demonstrated an extreme aversion to drinking water despite having exceedingly elevated serum sodium and serum osmolality levels. A variety of diseases has been associated with hypodipsic hypernatremia, including vascular abnormalities, neoplasms, granulomatous diseases, trauma, and ventricular cysts involving the

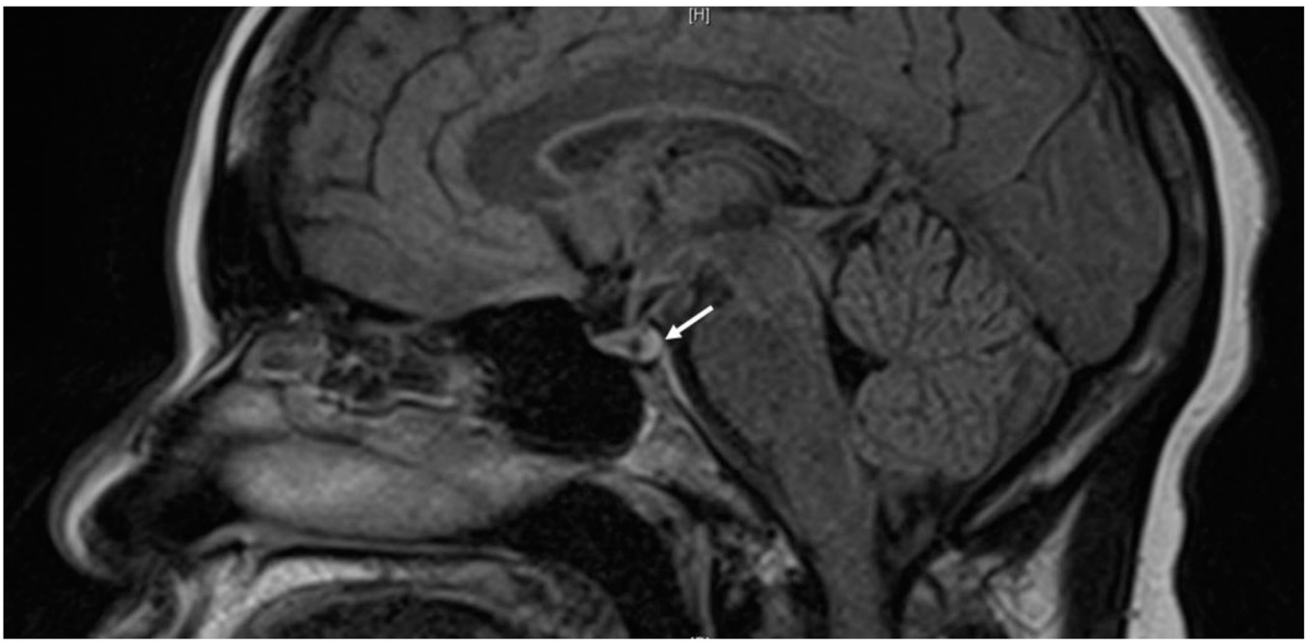

Figure 2. Sagittal view of brain MRI showing the bright signal (arrow) indicating intact AVP neurohypophysis.

hypothalamic region (1, 2). That her urine was concentrated during the attack strongly suggested that the hypernatremic dehydration had not resulted from excessive urinary water loss. Likewise, persistence of the posterior pituitary bright spot on the MRI scan indicated an intact posterior pituitary, which had retained AVP stores during the attack (7). These findings, however, did not indicate that her AVP secretion or hypothalamic osmoreceptors were normal. Other studies of adipsic hypernatremia have shown that osmotically mediated secretion of the hormone will be markedly deficient even when the response to nonosmotic stimuli is normal or even supranormal (1). The presence of the posterior pituitary bright spot suggested osmoregulation of her thirst and AVP secretion were both defective during the attack. The repeated hypernatremic episodes could be expected to reduce the pituitary AVP stores, thereby reducing the bright spot intensity normally emitted on T1-weighted MRI (7). That her urine osmolality was high but not at the expected levels during hypernatremic dehydration also suggested that osmotically stimulated AVP secretion was impaired during the episodes. The specific gravity during her first admission and before IV fluids were administered was 1.021, not the expected level if the AVP had been maximally secreted.

Psychiatric illness causing adipsic hypernatremia is an extraordinarily rare condition, and the few cases reported have all involved severe psychiatric illness (3–6). The location and nature of the etiology responsible for these defects in osmoregulation remain unknown; however, new diagnostic methods, such as functional MRI scans, have begun to identify areas in the brain related to psychogenic disorders and the sensation of thirst (8). Our patient had no known psychiatric illness; however, she did have a remote history of a similar episode and a reported depressed mood preceding the present admission. Her depressed mood and adipsia had resolved quickly with short-term therapy. Thus, a psychogenic cause of her adipsia is the most likely etiology. However, owing to the relatively short follow-up period, a more persistent defect in osmoregulation caused by a brain lesion undetected by the MRI could not be excluded. Thus, although certainly a very rare entity, psychogenic adipsic hypernatremia due to transient mood disorders should be considered in the differential diagnosis of hypernatremia.

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