

# Hyponatremic Encephalopathy after Excessive Water Ingestion Prior to Pelvic Ultrasound: Neuroimaging Findings

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## Abstract

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We report two patients with acute hyponatremic encephalopathy which developed after massive water ingestion for pelvic ultrasound and emphasize the findings of magnetic resonance (MR) imaging including diffusion-weighted imaging (DWI). Both subjects had completely recovered within 24 hours following fluid restriction and salt replacement. MR imaging revealed cortical sulcal narrowing, restricted diffusion and sulcal T2 hyperintensity along with diffuse pial enhancement suggesting diffuse cerebral cortical cytotoxic edema and blood-brain barrier breakdown. In addition to the first illustration of multimodality MR imaging features of water-intoxication, these two cases also highlight the need for standardized practice on the quantity of water intake recommended to distend the bladder for pelvic ultrasound, especially in patients at risk for serum inappropriate ADH syndrome-related hyponatremia.

**Key words:** water intoxication, acute hyponatremia, seizure, encephalopathy, serum inappropriate ADH syndrome, magnetic resonance imaging, diffusion-weighted imaging

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## Introduction

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Severe dilutional hyponatremia due to water intoxication is a serious, and potentially fatal (1, 2), situation resulting mostly in transient neurological dysfunctions such as confusion, headache, coma and epileptic seizures. The underlying pathology is hyponatremia-related cytotoxic brain edema. Water intoxication, also called overhydration is not an uncommon problem in intensive care units (3) due to direct overload of intravenous (IV) fluids and IV or enteral feeding with unbalanced amount of fluids given in mentally-depressed persons. In hyponatremic patients without dehydration and edema, serum inappropriate antidiuretic hormone (ADH) and cerebral salt wasting syndromes, severe hypothyroidism and glucocorticoid deficiency are encountered in

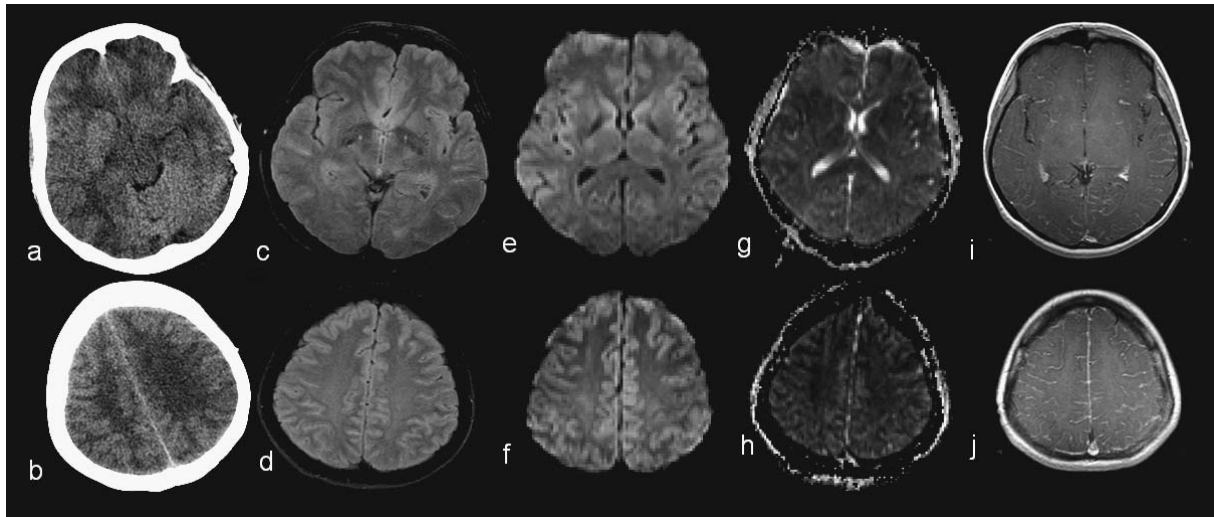
differential diagnosis in addition to water poisoning. Urine sodium concentration along with serum and urine osmolality differentiates water intoxication from the other entities. In contrast to that occurring in intensive care patients, water intoxication is extremely rare in subjects with a normal level of consciousness. Actually, under normal physical and nutritional conditions, there is a little reason for cognitively-healthy adults to worry about accidentally consuming too much water to cause intoxication (4-6). Psychogenic polydipsia spectrum disorders are the most frequent cause in these subjects (7). In addition, any activity or situation resulting heavy sweating, such as marathon running (8), can lead to water intoxication when excessive plain water is consumed to replace lost fluids. Iatrogenic symptomatic water intoxication caused by preparation for pelvic ultrasound in otherwise healthy subjects is a well-known, but ex-

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**Figure 1.** (Case 1) A non-enhanced cranial CT demonstrates narrowed sulci and ventricles. (a, b). Sulcal hyperintensities on FLAIR imaging (c, d) and widespread restricted diffusion of the cortical and subcortical gray and white matter on DWI and ADC maps (e-h) are shown. Extensive linear pial enhancement is seen on axial postcontrast T1-weighted MR imaging (i, j).

ceedingly rare, entity (9-14). On the clinical grounds, it cannot be distinguished from other forms of acute hypervolemic hyponatremia. We herein report two cases with this kind encephalopathy, who were investigated by MR imaging thoroughly. Although MR imaging characteristics of experimental hyponatremia-related cerebral edema has been recognized for a long time (15), no detailed human study on cases with hyponatremic encephalopathy or water intoxication has been reported in the literature to date.

## Case Report

### Case 1

A 33-year-old woman was presented to the emergency department (ED) in an unconscious state. Her relatives reported that she had been using escitalopram (10 mg at bedtime), which was prescribed for depression about 10 months previously, until 5 days before. For the last 5 days she had also been taking ornidazole for vaginal discharge. Four hours prior to her admission to ED of our institute, she had undergone a pelvic ultrasound for which she consumed 5-6 liter of regular water. She developed nausea and vomiting, and then numbness of her right arm, leg and upper lip. Soon after, she became progressively uncooperative and sleepy. Following a period of anxiety, diaphoresis and tremulousness, she had a generalized tonic-clonic seizure.

At admission, neurological examination showed that she had agitated confusion with no lateralizing signs. She was opening her eyes to verbal stimuli, but not responding meaningfully to any questions, or not obeying any simple commands. Physical examination was otherwise unremarkable.

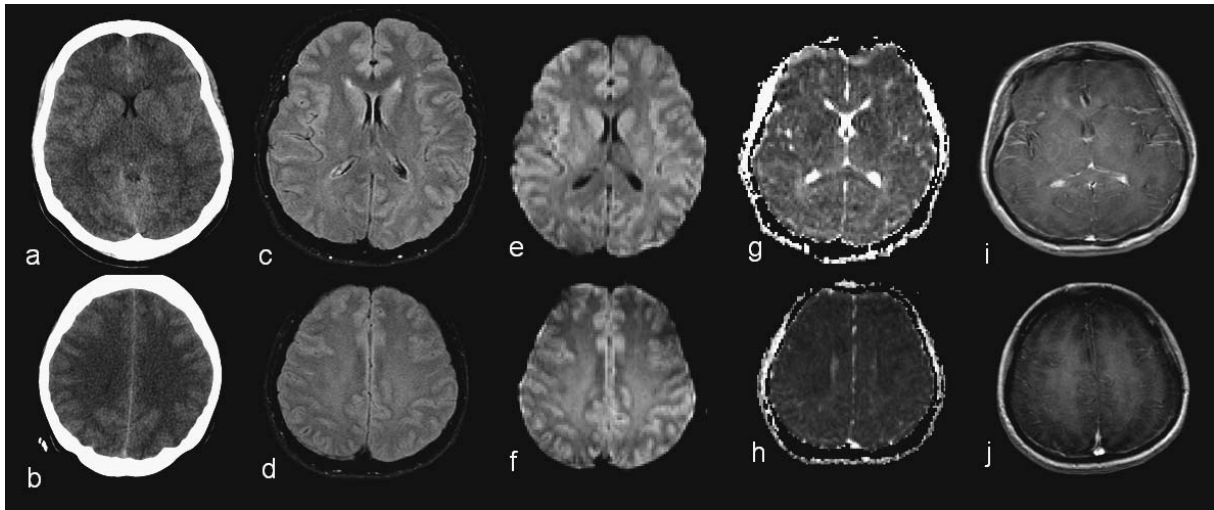
Emergency blood chemistry showed significant hyponatremia (122 mEq/L) and a low blood urea nitrogen (BUN)

level (4.6 mg/dL). Simultaneous urinary sodium was 83 mEq/L, with a serum and urinary osmolality of 285 and 186 mOsm/kg-water, respectively. Apart from a slight iron deficiency anemia (hemoglobin 10.7 g/dL), other blood tests were within normal limits. Of note, glucose, renal and liver function tests, cortisole, ACTH, TSH and thyroid hormone levels and arterial blood gases were normal.

A cranial computerized tomography (CT) (Sensation 16, Siemens Medical Solutions, Forchheim, Germany) scan, obtained 8 hours after symptom onset, demonstrated diffuse cerebral edema evident from narrowing of the hemispheric cortical sulci and the ventricles (Fig. 1a and b). A subsequent cranial MR (1.5 T scanner, Symphony, Siemens) imaging, obtained 14 hours after symptom onset, revealed sulcal hyperintensities on fluid attenuated inversion recovery (FLAIR) (TR/TE/TI; 8,150/125/2,150 ms) sequences (Fig. 1c and d). DWI (TR/TE; 2,800/78 ms, max b value of 1,000 s/mm<sup>2</sup>) and corresponding apparent diffusion coefficient (ADC) maps showed widespread restricted diffusion in cortices and subcortical white matter compatible with cytotoxic edema (Fig. 1e-h). Average cortical ADC values were measured in the range of 0.66-0.76×10<sup>-3</sup> mm<sup>2</sup>/sn. ADC (mm<sup>2</sup>/sn) was 0.75×10<sup>-3</sup> and 0.66×10<sup>-3</sup> in the basal ganglia and centrum semiovale, respectively. Extensive linear pial enhancement after contrast administration on T1-weighted (TR/TE; 600/20 ms) MR sequences indicates disruption of the brain-blood barrier (Fig. 1i and j). Perfusion-weighted MR imaging was normal (no picture presented).

A lumbar puncture showed normal protein (14 mg/dL) and glucose (55 mg/dL; simultaneous serum glucose; 75) concentrations in the cerebrospinal fluid (CSF). CSF microscopy and cultures were negative.

She responded well to a regimen of strict water restriction and oral salt supplementation, and eighteen hours later serum sodium levels returned to within normal range (137



**Figure 2.** (Case 2) A non-enhanced cranial CT shows diffuse sulcal effacement and compression of lateral ventricles (a, b). FLAIR imaging demonstrates obliteration of the cortical sulci and slit third and lateral ventricles. Widespread sulcal hyperintensities are also notable (c, d). DWI and ADC images indicate restricted diffusion over the cortices and subcortical white matter (e-h). Linear pial enhancement is present on axial postcontrast T1-weighted images (i, j).

mEq/L). Her symptoms resolved completely with no neurological sequela. Follow-up MR imaging with FLAIR, DWI, ADC and contrast-enhanced T1-weighted images, obtained 1 month later, showed no abnormality (no picture presented). Of note, ADC normalization was also documented numerically ( $0.96 \times 10^{-3} \text{ mm}^2/\text{sn}$  in temporal cortex and  $0.92 \times 10^{-3} \text{ mm}^2/\text{sn}$  in centrum semiovale).

## Case 2

A previously healthy 19-year-old female was brought to the emergency department with complaints of sudden-onset diffuse headache, nausea, vomiting, lassitude and progressive confusion. Symptoms developed almost two hours after a pelvic ultrasound, which was scheduled for her menstruation irregularities. Her family reported that she consumed almost 3 liters of regular water in 1.5 hours just before the scanning to fill the bladder full.

Neurological examination at admission showed lethargia along with slight central facial paresis and hemiparesis on the right. Physical and neurological examinations were otherwise in normal limits.

Significant hyponatremia (126 mEq/L) along with slight hypokalemia (3.4 mEq/L) and anemia (hemoglobin: 11.2 g/dL) was detected. Serum and urine osmolality were 262 and 192 mOsm/kgwater. Urine sodium was less than 10 mEq/L. Results of other blood test including glucose, liver and renal function tests as well as arterial blood gases and toxicity screen were within normal limits.

Emergent cranial CT (Sensation 16, Siemens Medical Solutions), obtained 2 hours after symptoms onset, showed diffuse sulcal effacement and compression of lateral ventricles consistent with brain edema (Fig. 2a and b). A brain MR imaging was obtained approximately 8 hours later on a 1.5 T scanner (Symphony, Siemens). FLAIR (TR/TE/TI; 8,500/

98/2,150 ms) sequences also demonstrated obliteration of the cortical sulci and slit third and lateral ventricles. Widespread sulcal hyperintensities were also notable (Fig. 2c and d). DWI (TR/TE; 2,800/78 ms, max b value of 1,000  $\text{s}/\text{mm}^2$ ) and ADC images indicated widespread mild restricted diffusion in the cortical and deep gray matter as well as in the centrum semiovale (Fig. 2e-h). ADC values were measured  $0.61 \times 10^{-3} \text{ mm}^2/\text{sn}$  in the frontal lobe cortex,  $0.69 \times 10^{-3} \text{ mm}^2/\text{sn}$  in the centrum semiovale and  $0.73 \times 10^{-3} \text{ mm}^2/\text{sn}$  in the putamen on the right. Albeit the presence of a slight motion artifact, significant pial contrast enhancement was discernible in T1-weighted (TR/TE; 600/20 ms) images, indicating brain-blood barrier disruption (Fig. 2i and j). Cerebral MR venography and angiography were normal (no picture given).

A lumbar puncture performed later showed a normal glucose level (58 mg/dL, simultaneous blood glucose: 58 mg/dL) and protein levels (15.3 mg/dL) in the CSF. No cell and microorganism were observed on direct microscopy of CSF.

Her status was recovered dramatically in parallel with the gradual rise of serum sodium concentration in about sixteen hours (up to 136 mEq/L). After 48 hours observation, she was discharged from emergency unit with normal neurological findings. Thyroid function tests, serum cortisole and ACTH levels obtained then were within the normal limit. Blood and urine osmolality increased to 292 and 981, respectively. Urine sodium was 82 mEq/L. She had no complaints since then (almost 2 years later). No follow-up MR imaging was pursued.

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## Discussion

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We describe two previously healthy women with hyponatremic encephalopathy which developed after excessive

water ingestion in a relatively short time period for pelvic ultrasound examination. Routine blood examination revealed hyponatremia and slightly low hematocrit. Water intoxication was suggested by the results of urine sodium along with serum and urine osmolality. However, as in the cases herein presented, discrimination of water intoxication and serum inappropriate ADH syndrome may always not be so easy. Serum inappropriate ADH syndrome is characterized by inappropriately concentrated urine (urine osmolality above 150 mOsm/kg-water) with ongoing natriuresis (urine sodium higher than 20 mEq/L) against hypotonicity of plasma (plasma osmolality below 280 mOsm/kgwater). In contrast, urine osmolality (usually less than 100 mOsm/kgwater), urine sodium (less than 10 mEq/L) and plasma osmolality (less than 280 mOsm/L) are all reduced in water intoxication. In both cases, urine osmolality was less than serum osmolality indicating excessive water excretion. Urinary sodium excretion was within the normal limits, or not increased, in the first case, and it was significantly decreased in the second one. Therefore, moderate water intoxication, associated with chronic underlying serum inappropriate ADH syndrome in the first case, was considered in both. There was no apparent risk factor for serum inappropriate ADH syndrome in the first case. Although the association of hyponatremia with selective serotonin receptor inhibitors including escitalopram (16-19) has been well recognized, it is unlikely to occur in the absence of additional risk factors other than being a lean female and following cessation of escitalopram after 9-month usage.

Water intoxication originates from a relatively rapid intake of a large volume of parenteral and/or oral fluid without electrolytes in excess of the renal excretion capacity in a short period of time. Healthy kidneys are able to excrete approximately 1 liter of fluid per hour (20), and therefore excessive fluid results in retention. To eradicate iatrogenic water intoxication, or dilutional and hypotonic hyponatremia in other terms, in association with medical procedures requiring a full bladder such as a pelvic ultrasound or uroflowmetry, a new recommendation strategy seems to be necessary as opposed to the common "as much as possible" advice. If health care personnel state that "the more you drink, the better the test results", patients may intake several fold higher amounts. As supported by our experience with these two cases, the amount of water necessary to guarantee sufficient distention of the bladder should be limited to 1 liter ingested 1 hour before the procedure to exclude the risk of this potentially significant adverse event. This advice should invariably be in written form. Another important related point is that with stress, anesthesia, prolonged physical activity and several disease states, such as those with inappropriate ADH secretion reduce renal excretion capacity, significant retention can occur after intake of much smaller volumes of free water. Therefore, in patients who are at risk of serum inappropriate ADH syndrome such as those taking risky medications, pelvic ultrasound examination can be performed via alternative routes such as transvaginally when

convenient (13) or the bladder can be filled retrogradely by means of a urinary catheter.

In addition to these practical points, MR features of dilutional hyponatremia are unprecedentedly documented through the present cases. Brain edema and disruption of brain-blood barrier (BBB) permeability seem to be the two main MR characteristics of dilutional hyponatremia which merit discussion.

Decreased circulating osmolality resulting from acute dilutional hyponatremia does not affect, at the same time, the osmolality of cerebral extracellular space. Therefore, an osmotic gradient across the BBB is generated. Acting as a semi-permeable membrane, intact BBB will allow water transport into cells and eventual cytotoxic brain edema. With T1- and T2-weighted MR imaging, brain edema is reflected in parenchymal swelling and thus effacement of the sulci and ventricles. However, with these conventional MR modalities radiological diagnosis of mild to moderate cerebral edema is difficult, if not impossible, because the mass effect is usually faint and can be overlooked. DWI, on the other hand, not only shows edema promptly but also differentiates cytotoxic edema from the vasogenic type thus underlying tissue changes. Experience with acute stroke cases indicates that DWI shows restricted diffusion within minutes after the development of ischemic cytotoxic edema. Cytotoxic edema produces DWI bright and ADC dark parenchymal changes and/or lesions which are easily noticeable. Albeit not frequently documented in humans, DWI appearance of hyponatremic cerebral edema is analogous to its ischemic counterpart. In a hyponatremia rat model produced with water intoxication, similar to the acute stroke, a close correlation between the decrease of brain ADC and increase of total brain water content was demonstrated (15). In both of the present cases, a widespread cortical and subcortical cytotoxic edema was unobjectionably demonstrated. Interestingly, these DWI lesions are reversible, which was confirmed by MRI in one of them. Even though edema-related swelling of perivascular astrocytic foot processes can result in cerebral ischemic damage via impeding microcirculation, this is not the case in hyponatremic encephalopathy when brain adaptation is not impaired.

In the present cases, the increase of BBB permeability was documented by leptomeningeal enhancement on gadolinium-enhanced T1-weighted images and widespread sulcal hyperintensities on FLAIR imaging suggested protein escape into CSF spaces. BBB status has been studied in various experimental models of hypoosmotic hyponatremia including water intoxication. However, no consensus was attained with these studies: early studies showed no change of BBB permeability (21), while, later studies demonstrated transiently increased permeability (22). Other reasons of thin, linear leptomeningeal enhancement include meningeal inflammation, irritation and hyperemia. However, since the laboratory and clinical findings were apparent and reversible in our patients, no further investigation was performed. Albeit status epilepticus may lead to a similar appearance, this

can not be attributable to a single seizure. However, the correction of hyponatremia, especially when rapid, can disrupt BBB permeability in some particular brain areas which did not occur in our cases.

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