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Case Report

A case in which water intoxication due to excessive water ingestion did not inhibit the secretion of arginine vasopressin

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SUMMARY

We experienced a case of water intoxication due to excessive water ingestion that was complicated by the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). A 60-year-old Japanese woman with nervous depression drank too much lemon tea within several hours, vomited ten times, and developed disturbed consciousness and dysarthria. Her plasma arginine vasopressin (AVP) concentration was not inhibited, although her plasma osmolality was low. Nausea and/or stress may stimulate AVP secretion regardless of the hypo-osmolality. We believe that dilatation of her stomach due to excessive liquid ingestion and cerebral edema due to hypo-osmolality brought on her nausea. Stress induced by a psychiatric problem and/or admission to a hospital may also stimulate AVP secretion by the central nervous system. Treating nausea and stress may help reduce AVP secretion and resolve hyponatremia.

Key Words : excessive water ingestion, nausea, arginine vasopressin (AVP), mental stress

INTRODUCTION

Excessive water ingestion sometimes leads to water intoxication in which hyponatremia causes fatal cerebral edema. Water intoxication is a disorder that causes euvolemic hypotonic hyponatremia. Water intoxication due to excessive water ingestion needs to be differentiated from the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Most patients with water intoxication due to excessive water ingestion have very low levels of arginine vasopressin (AVP) and a urine osmolality that is very low (less than 100 mOsm/L). By contrast, a patient with SIADH has high AVP levels and a high urine osmolality (greater than 500 mOsm/L)[1]. However, there are some recent cases in which water intoxication due to excessive water ingestion seems to be complicated by SIADH[2~4]. We report a case of water intoxication complicated by SIADH, which occurred after a patient drank too much lemon tea. We also discuss why it is possible for these two opposing pathophysiological processes to coexist.

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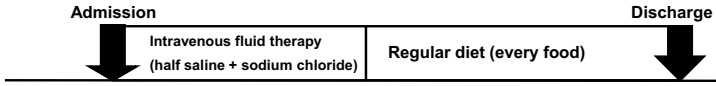
CASE REPORT

A 60-year-old Japanese woman presented with disturbed consciousness, dysarthria, faintness, and nausea. She had been diagnosed with nervous depression and



Day	1	2	3	4	5	6	7	8	9	10	11	1 month later	
Na^+ intake	99	293	302	249	249	77							mEq
Water intake	500	3000	2500	2000	2000	500							mL
Urine output	330	2290	2740	2556	1884	1190	1083	1105	627	700			mL
Serum Na^+	109	122	123	125	122	125	130	133	135	138	140	138	mEq/L
Serum K^+	3.3	2.6	2.9	3.3	3.0	3.5	3.4	3.0	3.0	3.4	3.6	4.7	mEq/L
Serum Cl^-	70	80	88	90	88	91	98	97	101	103	104	100	mEq/L
Plasma Osm		235	247	248	248	250	260	265	274	278	286	291	mOsm/L
Plasma AVP			2.3			1.4							pg/mL
Urine Na^+	36				135	160	207	227	83	153	224		mEq/L
Urine Osm		283			395	496	682	648	600	469	648		mOsm/L

Fig. 1 Clinical course

treated with nitrazepam for several years as a psychiatric outpatient. She seldom drank alcoholic beverages, and she smoked 40 cigarettes per day. There was no history of polydipsia. Her family history was unremarkable.

In September 2009, she drank too much lemon tea within several hours. She then vomited ten times, and presented with dysarthria and faintness. Two days after her polydipsia, her family came home by chance and found her in a disturbed state of consciousness with fifteen, two liter plastic bottles which were empty (30 liters). They observed her behavior for one day ; however, she did not improve. She was subsequently admitted to a room in the emergency division of our hospital.

On admission, she was in a comatose state, but responded to painful stimulus by brushing away the examiner's hand. Her blood pressure was 128/82 mmHg ; heart rate, 94 beats per minute and regular ; and respiratory rate, 24 breaths per minute with snoring-like breathing. Body temperature was 35.7°C. There was no sign of dehydration. There was no edema in her limbs. Heart sounds were clear and heart rhythm was regular without audible murmurs or friction sounds. Breath sound was normal and without crackles or wheezes. The abdomen was flat and soft, and bowel sounds were normal. Pupils were equal and mildly dilated but reactive to light. She spoke thickly and had difficulty in speech. There was no sign of motor or sensory palsy.

Arterial blood gas analysis revealed a pH of 7.583 ; PaO_2, 88.6 mmHg ; $PaCO_2$, 29.2 mmHg ; and HCO_3^-, 26.9 mEq/L under room air. Her hematological values were hemoglobin, 12.7 g/dL ; hematocrit, 32.7% ; red blood cell count, $376\times10^4/\mu$L ; white blood cell count, 10,900/μL. Her level of aspartate amino transferase was 66 IU/L ; alanine transaminase, 23 IU/L ; lactate dehydrogenase, 470 IU/L ; total bilirubin, 1.5 mg/dL ; total protein, 6.3 g/dL ; albumin, 3.75 g/dL ; blood urea nitrogen, 6.0 mg/dL ; creatinine, 0.4 mg/dL ; creatine kinase, 2790 U/L ; creatine kinase-MB fraction, 38.5 U/L ; C-reactive protein, 4.5 mg/dL ; and glucose, 91 mg/dL. Her serum electrolyte values were : sodium, 109 mEq/L ; potassium, 3.3 mEq/L ; chloride, 70 mEq/L ; and calcium, 9.0 mg/dL. The anion gap was 12.1. On the second day, her plasma osmolality (actual value) and urine osmolality were 235 mOsm/L and 283 mOsm/L, respectively.

The endocrinological aspect was studied on the third day. Her blood data did not indicate adrenal insufficiency ; her basal plasma cortisol concentration was 21.4 μg/dL and ACTH was 15.4 pg/mL. The data indicated a non-thyroid illness (FT_4, 1.49 ng/dL ; FT_3, 1.22 pg/ml ; TSH, 1.17 μU/mL) and inappropriate secretion of AVP (plasma AVP concentration, 2.3 pg/mL ; plasma osmolality 247 mOsm/L).

Head, chest, and abdominal computed tomography showed unremarkable findings. An electrocardiogram was within normal limits.

She was diagnosed as having water intoxication. Intravenous fluid therapy (half saline + sodium chloride) from day 1 to day 6 was administered in the intensive care unit (Fig. 1). She improved gradually. On the fourth day, her consciousness was completely clear and she was able to speak without difficulty. On the third and the sixth days, her plasma AVP secretion

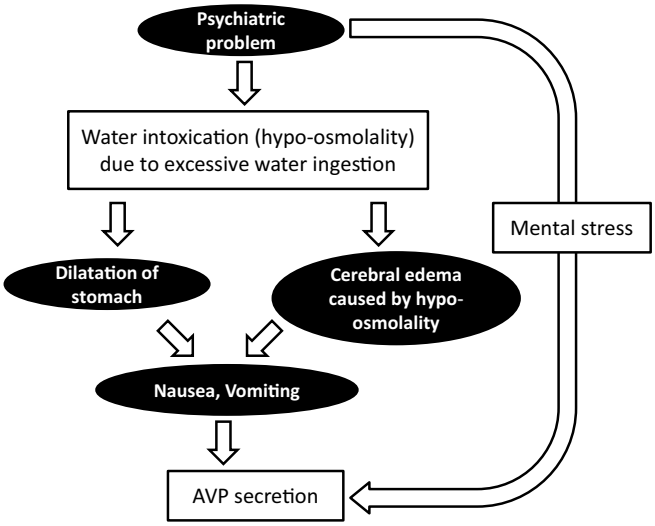


Fig. 2 Possible mechanism of AVP secretion under low plasma osmolality

was not inhibited despite a low plasma osmolality. She began a regular diet without water restriction on the sixth day. She did not drink too much water, and was discharged on the eleventh day. In a one-month follow-up after discharge, her serum concentrations of sodium and plasma osmolality were within normal limits without episode of polydipsia.

DISCUSSION

AVP secretion is ordinarily inhibited when the plasma osmolality is below 275 mOsm/L[5]. In the present case, AVP secretion was not inhibited, although the plasma osmolality was 247 mOsm/L. Therefore, we could not help concluding that this patient had inappropriate AVP secretion. A urine osmolality that exceeds the plasma osmolality is compatible with SIADH. But the patient's history of drinking too much lemon tea within several hours indicated water intoxication due to excessive water ingestion.

Is it possible for the opposing pathogeneses of water intoxication due to excessive water ingestion and SIADH to coexist? There are some cases of water intoxication due to excessive water ingestion coexisting with SIADH that was caused by the use of certain drugs such as "ecstasy"[6,7], fluoxetine[8], and oxcarbazepine[9]. Among these candidate drugs, our patient had taken only nitrazepam. As far as we know, there are no reports of nitrazepam being associated with water intoxication or SIADH. It is well accepted that there is an insufficient inhibition of AVP secretion after a water load in schizophrenic patients with compulsive water drinking[10]. Water intoxication due to excessive water ingestion and SIADH can also coexist in other types of psychiatric patients[11,12]. On the other hand, the coexistence of water intoxication and SIADH has been seen in non-psychiatric patients[2~4]. Therefore, the coexistence of water intoxication due to excessive water ingestion and SIADH is not attributable only to psychosis.

Is it possible that there was not enough time for hypo-osmolality to inhibit AVP secretion in our patient? The half-time of AVP is 5.6 minutes[13]. When the plasma AVP was studied in our patient, four days had already passed from the episode of excessive ingestion of lemon tea. Therefore, we believe that there was enough time for hypo-osmolality to inhibit AVP secretion in our patient.

We emphasize that nausea plays an important role in the development of SIADH with water intoxication due to excessive water ingestion (Fig. 2). Nausea is probably the most potent factor for stimulating AVP secretion, leading to as much as a 500-fold rise in circulating AVP levels[14]. Excessive water ingestion initially leads to nausea because of a full stomach. In humans, the volume of the empty stomach is 200 mL and the volume of the stomach 30 minutes after a solid meal is 787 mL[15]. It is not well understood how much liquid is needed to mechanically cause nausea, but we can definitively say that a liquid volume exceeding the stomach's volume can cause nausea and/or vomiting.

In our patient, the ingestion of 30 liters of lemon tea within several hours is believed to have been enough to induce nausea mechanically. In addition, hypo-osmolality caused by willfully ingesting excessive water can lead to cerebral edema, which then induces nausea.

It is generally accepted that stress is a cause of AVP secretion[16,17]. With excessive water ingestion, stress may also play a role in AVP secretion (Fig. 2). AVP secretion is ordinarily inhibited in hypo-osmolality. However, there may be some patients in whom the stress-induced stimulation of AVP secretion exceeds the inhibition of AVP secretion by hypo-osmolality.

One hypothesis proposes that plasma AVP concentration may prove to be an objective marker for nausea[18]. However, how long nausea and vomiting have to persist to bring about hyponatremia has not been well established[19]. Further study is required to determine whether some anti-emetics can inhibit AVP secretion. Treating stress may reduce AVP secretion. Based on these concepts, more investigations are needed to determine whether anti-anxiety medications (which do not induce SIADH) could be effective in the medical treatment of SIADH.

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