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WATER INTOXICATION IN A DRUG-FREE SCHIZOPHRENIC PATIENT

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Abstract: A 27-year-old woman with schizophrenia disorder developed water intoxication due to primary polydipsia in drug-free state. Manner of vasopressin secretion was investigated with water loading and hypertonic saline infusion. The sensitivity of vasopressin secretion response to changing osmolality was low in this patient, which might be involved in the occurrence of water intoxication, linked to Type IV SIADH.

Index Terms

schizophrenia, water intoxication, vasopressin, SIADH

INTRODUCTION

The syndrome of water intoxication is a distinct clinical entity that occurs almost exclusively in patients with chronic mental disorders. The essential mechanism of this syndrome is rapidly progressive profound hyponatremia due to polydipsia with excessive water intake, leading to brain edema with neurological and psychiatric symptoms. Since excessive water intake alone is rarely sufficient to produce marked hyponatremia, water intoxication has been linked to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH)[1,2,3]. In epidemiological surveys[4], the factors found to be most widely associated with water intoxication have been chronicity, certain psychiatric disorders, smoking, and drugs that decrease the excretion of free water. From the results of an epidemiological study on hyponatremia[5], it was suggested that the pathogenesis of hyponatremia in psychiatric patients might be involved in a chronic course and poor response to psychopharmachotherapy. Generally water intoxication is regarded as one unfavorable of result from psychophamachotherapy. We experienced a case of water intoxication in a drug-free patient and studied arginine vasopressin secretion in this patient.

CASE HISTORY

Y was a 27-year-old woman and the second of two children, with no family psychiatric history. She complained of inattention during her fourth year of college. She withdrew from work and was noted at age 23 to be withdrawn, associating loosely, inattentive, disheveled and blunted. At age 26 she developed agitation and bizarre behaviors with hallucinations and delusions. She drank copious volumes of water and bathed herself almost two hours everyday. The major reasons she had to explain her behavior included "cleansing herself" and "washing

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out the poisons". In spite of her psychotic symptoms, she had not received any psychiatric attention and treatment. She threw bottles and attacked her family with a knife. She was taken into custody by the police and admitted to the Psychiatric Service of Kijima Hospital. At the initial interview, she was observed to be unkempt and incoherent. On examination, her pulse 72/min of low volume, blood pressure 130/70, and the abdomen slightly distended, with no rigidity or tenderness.

Four hours after admission, she vomited twice, and her level of consciousness was lowered (Japan Coma Scale "200"), which was followed by two grand mal fits; Head CT showed brain edema (Fig. 1), EEG showed minimal excess of diffuse, sporadic theta activity over both hemispheres (Fig. 2), consistent with a metabolic toxic state, and serum results were : Na 115 mEq/L (135-145), Cl 76 mEq/L (98-108), K 2.7 mEq/L (3.5-5.1), Blood urea nitrogen 1.8 (2.4-6.0). (Normal values in brackets). The above results were consistent with a diagnosis of water intoxication, secondary to psychogenic polydipsia. The serum arginine vasopressin was not assayed.

The treatment on the first day consisted of intravenous administration of maintenance fluid (Physiosol-3® 1,000 ml, glycerol 400 ml, isotonic sodium chloride solution, 1,000 ml. The patient excreted 5,980 ml of urine over 12 hours on the first day. On the 2 nd day, serum sodium level was 128 mEq/ml, the same treatment was repeated, and her consciousness level returned to "100" (Japan Coma Scale). On the 3 rd days, her consciousness level became normal ("O" by Japan Coma Scale) and auditory hallucinations and delusions of persecution became evident. She was advised to undergo extended psychiatric treatment, including the use of psychotropic medication. She refused and demanded release from the hospital. Since she and her family claimed to understand the danger of her conduct, she was advised to visit the Psychiatric

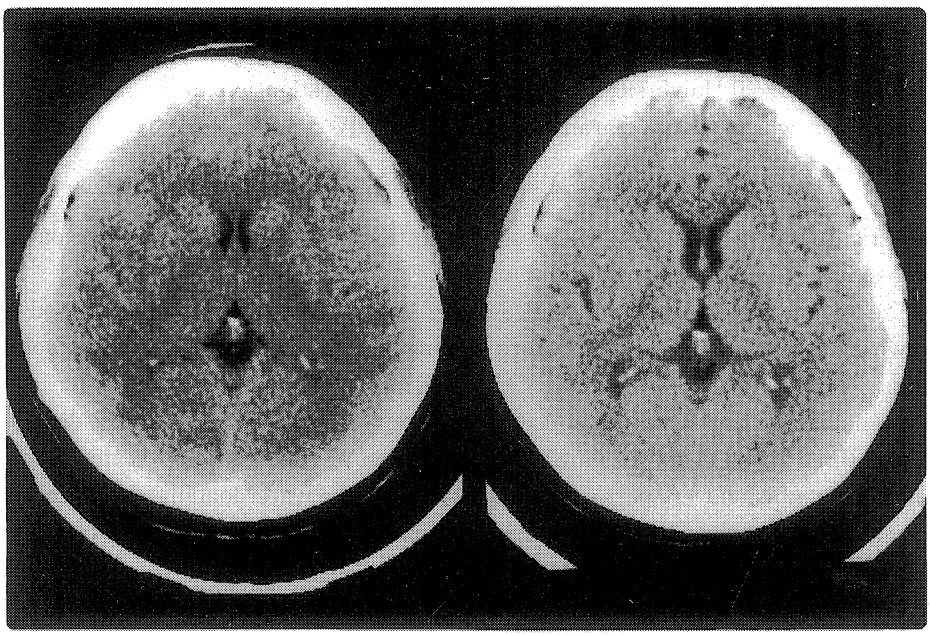

Fig. 1. left ; Syluvian fissure and lateral ventricles are almost disappeared, right ; normal image after recovery from water intoxication.

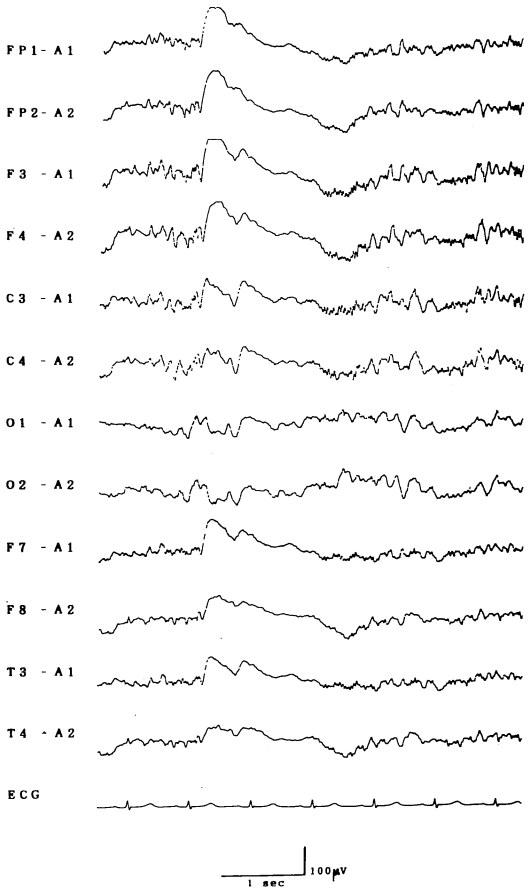

Fig. 2. 10 Herz generalized α activity with small amount of sporadic θ waves is consistent with a metabolic toxic state.

Service of Nara Medical University Hospital for further investigation and treatment. The case was diagnosed as schizophrenia, paranoid type on DSM IV criteria.

MANNER OF VASOPRESSIN SECRETION

To investigate the manner of vasopressin secretion in this patient, water loading and hypertonic saline infusion were performed.

Water (20 ml/kg body weight) was loaded orally over a period of 15 min, and blood samples were drawn from an antecubital vein before loading and 30 min and 60 min after completion of loading.

3 % sodium chloride of 660 ml was infused over 50 min, and blood samples were drawn before infusion and three times every 20 min after completion of the infusion. Water loading and hypertonic saline infusion were performed separately. At the water loading, the patient had not been medicated. But she was treated with halopridol 5 mg/day at the time of hypertonic saline infusion. This patients was a non-smoker.

Plasma vasopressin level, plasma osmolality, and serum sodium concentration were determined[6]. The results are shown in Table 1 and Fig. 3. There was a significant correlation between plasma osmolality (X mosmo/kg) and plasma vasopressin (Y pg/ml), with a regres-

Table 1. Osmolality and vasopressin level in plasma of the patient

Time [min]	Na [mEq/L]	Osm [mOsm/kg]	VP [pg/ml]
Water loading test			
0	133	280	0.3
30	131	283	0.3
60	136	295	0.3
Hypertonic saline infusion			
0	139	290	0.9
20	147	308	1.3
40	145	308	1.1
60	145	308	1.4

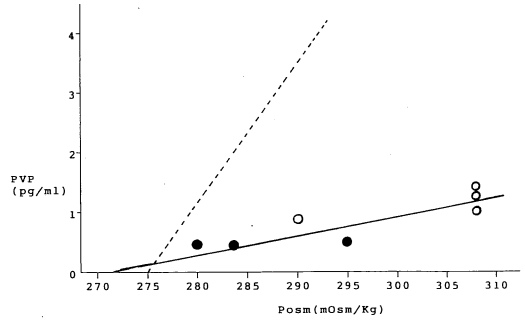

Fig. 3. Relationship of plasma vasopressin (PVP) to plasma osmolality (Posm). Open circle: with hypertonic saline infusion, solid circle: with water loading. Regresstion line in this patient is Y=0.035(X-272), Regression line in normal population in Y=0.23(x-275), which is dotted.

sion line of Y=0.035 (X-272), r=0.86. The slope of the regression line represents the sensitivity of vasopression secretion to changing osmolality. The X-intercept represents the threshold of the osmostat. Compared with the regression line of the normal population, Y=0.23 (X-275)[7], the slope of this patient was decreased and the X-intercept was almost same.

DISCUSSION

The maintenance of plasma volume and osmolality is a finely regulated process involving integration of thirst sensation and release of vasopression, a hormone produced by the paraventicular and supraoptic nuclei of the hypothalamus. Osmoreceptors supposedly located in the anteroventral third ventricle[8], are able to detect small changes in the circulating plasma osmolality and control both thirst and vasopressin secretion in a very logical manner. SIADH can be defined as an aberrant state characterized by abnormalities of osmoregulation of plasma vasopressin secretion[6], i. e. in SIADH, plasma vasopressin is inappropriately secreted through abnormal osmoregulation.

We found in a previous study that the sensitivity of the vasopressin secretion response to changes in osmolality was decreased in medicated schizophrenic patients[6] and that one type of water intoxication in medicated schizophrenic patients with polydipsia involved in Type IV SIADH (hypovasopressinemic antidiuresis)[9], linked with atrial natriuretic peptide secretion[10]. This mechanism of kidney inability to excrete free water might be explained as a low sensitivity of vasopressin secretion response to osmotic change and secondary renal hypersensitivity to vasopressin.

This study that the low sensitivity of vasopressin secretion response was found in this patient who had developed water intoxication in a drug free state. Also these results suggest that this mechanism of water intoxication in this patient might be involved in Type IV SIADH. Vieweg et al.[11] have described patients with Type I SIADH with water intoxication. Hariprasad et al.[3] suggested a diagnosis of Type II SIADH in a patient with hyponatremia and polydipsia.

Delva et al.[12] demonstrated that out of nine patients with polydipsia, seven had Type I SIADH and two had Type II. These findings indicate heterogeneity among psychiatric patients as to the presence and subtype of SIADH, suggesting that psychotic illness itself may sometimes be associated with SIADH.

The present results indicate nothing about assessing polydipsia in schizophrenic patients. Water intoxication with mental disorders should be consisted of polydipsia and SIADH. Further studies are needed to confirm the factors causing polydipsia and to ascertain whether psychosis itself is fundamentally involved.

REFERENCES

1) **Ajlouni, K., Kern, M. W., Tures, J. E., Theil, G. B.** and **Hagen, T. C.**: Thiothixene-induced hyponatremia. Arch. Intern. Med. **134**: 1103-1105, 1974.

2) **Raskind, M. A., Orenstein, H.** and **Christopher, G.**: Acute psychosis, increased water ingestion, and inappropriate antidiuretic hormone secretion. Am. J. Psychiatry **132**: 907-910, 1975.

3) **Hariprasad, M. K., Eisinger, R. P., Nadler, J. M., Padmannabhan, C. S.** and **Nidus, B. D.**: Hyponatremia in psychogenic polydipsia. Arch. Intern. Med. **140**: 1639-1642, 1980.

4) **de Leon, J., Verghese, C., Tracy, J. I., Jossiassen, R. C.** and **Simpson, G. M.**: Polydipsia and intoxication in psychiatric patients: a review of the epidemiological literature. Biol. Psychiatry **35**: 408-419, 1994.

5) **Ohsawa, H., Kishimoto, T., Hirai, M., Shimayoshi, N., Matsumura, K., Oribe, H., Hirao, F., Ikawa, G., Nakai, T., Miyake, M.** and **Kurata, S.**: An epidemiological study on hyponatremia in psychiaric patients in mental hospitals in Nara Prefecture. Jpn. J. Psychiatry Neurol. **46**: 883-889, 1992.

6) **Kishimoto, T., Hirai, M., Ohsawa, H., Terada, M., Matsuoka, I.** and **Ikawa, G.**: Manners of arginine vasopressine secretion in schizophrenic patients - with reference to the mechanism of water intoxication. Jpn. J. Psychiatry Neurol. **43**: 161-169, 1989.

7) **Tokinaga, K., Terano, T.** and **Yoshida, S.**: Vasopressin (anti-diuretic hormone: ADH). Nippon Rinsho **53**: 304-307, 1995.

8) **Bealer, S. L., Phillips, I., Johnson, A. K.** and **Schmidt, P. G.**: Anteroventral third ventricle lesions reduce antidiuretic responses to angiotensin II. Am. J. Phsiol. **236**: E 610-E 615, 1979.

9) **Zerbe, R., Stropes, L.** and **Robertson, G.**: Vasopreessin function in the syndrome of inappropriate antidiuresis. Ann. Rev. Med. **31**: 315-327, 1980.

10) **Ohsawa, H., Kishimoto, T., Shimayoshi, N., Matsumura, T., Tahara, K., Kitera, K., Higashiura, N., Noriyama, R., Matsumoto, H., Hirai, M.** and **Ikawa, G.**: Atrial natriuretic peptide and arginine vasopressin secretion in schizophrenic patients. Acta Psychiatrica Scand. **88**: 130-134, 1993.

11) **Vieweg, W. V. R., Riwe, W. T., David, J. J., Curnow, R. T.** and **Spradlin, W. W.**: Self-induced water intoxication and psychosis (SIWIP): Subcategory of the syndrome of inappropriate antidiuresis (SIAD). Psychiatry Med. **4**: 277-290, 1987.

12) **Delva, N. J., Crammer, J. L., Lawson, J. S., Lightman, S. L., Sribney, M.** and **Weir, B. J.**: Vasopressin in chronic psychiatric patients with primary polydipsia. Br. J. Psychiatry **157**: 703-712, 1990.