

## Case report

# A Successful Treatment of Primary Polydipsia with Topiramate

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**Abstract:** The patient is a 73 year-old woman who was hospitalized in the internal medicine ward for diarrhea, vomiting, and loss of balance. The blood sample showed hyponatremia. Polydipsia was suspected because she consumed 4-5 liters of water a day. The hormonal examination in the blood and urine including thyroid and adrenal functions showed no abnormalities. After limitation of water intake, the sodium level in the blood was improved and then she was discharged from the hospital. Although she visited a university hospital and a psychiatric hospital, the cause was not elucidated. Her husband took her to our hospital as an outpatient because she started to take excessive water intake at home again. She was hospitalized in our hospital and the water intake was restricted. She was diagnosed as primary polydipsia. The treatments including antidepressants, angiotensin-converting enzyme inhibitors, quetiapine, olanzapine, and risperidone were not effective. The treatment of topiramate was tried to inhibit her impulse of water intake. Her impulse was remarkably reduced and she was discharged to her home. She is being followed as our outpatient without excessive water intake.

**Key Words:** primary polydipsia, hyponatremia, topiramate

## INTRODUCTION

Primary polydipsia, a disorder caused by a primary increase in thirst, is most often seen in patients with psychiatric illness<sup>1-6)</sup>. One study of 239 hospitalized patients with mental illness found that 6.6 percent had a history compatible with compulsive water drinking and one-half of these had intermittent symptoms of hyponatremia due to transient water retention<sup>7)</sup>. Although it is often related to schizophrenia and the side effect of antipsychotics, it also has been reported in patients with affective disorders,

mental retardation, alcoholism, and brain injuries<sup>4,8)</sup>. The excessive water intake results in hyponatremia. Mild hyponatremia causes nausea, malaise, headaches, lethargy, and obtundation, while seizures, coma, and respiratory arrest occur with severe hyponatremia because of cerebral edema due to a decrease in serum osmolality which causes water movement into cells.

The treatment consists of water restriction, behavioral interventions (seclusion or restrains), and medications<sup>9-11)</sup>. Patients who cannot understand their illness, especially schizophrenia could require long-term hospitalization owing to polydipsia. The medications to treat polydipsia include propranolol, angiotensin-converting enzyme inhibitors, angiotension II receptor antagonists, olanzapine, risperidone, clozapine, phenytoin, demeclocycline, naloxone, antide-

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pressants, clonidine, vasopressin receptor antagonists, and acetazolamide<sup>12–19</sup>).

Topiramate is basically an anticonvulsant which blocks neural voltage-dependent sodium channels, enhances GABA(A) activity, antagonizes AMPA/kainate glutamate receptors, and weakly inhibits carbonic anhydrase. It is used for migraines<sup>20</sup>), alcohol dependence<sup>21</sup>), binge eating disorder<sup>22</sup>) as well. In addition, there is a report that it was successfully used for polydipsia due to schizophrenia<sup>23</sup>). However, there are no reports of its use for primary polydipsia without schizophrenia so far. Here I will report a first case that topiramate is effective for primary polydipsia without schizophrenia.

#### CASE REPORT

Patient: 73 years old, female

Chief complaint: Excessive water intake (4–5 liters)

Past medical history: Osteoporosis

Past surgical history: Right femoral neck fracture (2014), vertebral compression fracture (2015), right proximal humeral fracture (2016)

Present medical history: In 2014, she suddenly started to have poor appetite and did not eat food orally. Her husband took her to a public hospital, a university hospital, and a private psychiatric hospital. However, the cause could not be identified. Since she and her husband hoped to stay at home, visiting nursing care was introduced. She refused to have the care and was eating only small amount of food her husband cooked. In March, 2016, she had a fall and was hospitalized because of the right proximal humeral fracture. Her weight went down to 26.9 kg. In August, 2016, she suddenly started to have an urge to take excessive water and then had vomiting and diarrhea. She was hospital-

ized in the ward of internal medicine at a public hospital because of hyponatremia. The medical cause was not found out. Two weeks later she was discharged and referred to a psychiatric hospital if she had polydipsia again. She was taken to our hospital as an outpatient on September 12<sup>th</sup>, 2016, and hospitalized on the same day because of recurrent primary polydipsia and anorexia.

On examination at hospitalization, the blood pressure was 120/79 mmHg, the pulse 85 beats per minute, the body temperature 36.8 C, the oxygen saturation 96% while the patient was breathing ambient air. The patient was in a wheelchair. The height was 150 cm, the weight 28.6 kg, and the BMI 12.71. The orientation for date, place, and person was clear. She seemed to have no hallucination, delusion, depression, or anxiety. The oropharynx had no erythema or exudate. The conjunctivae were neither anemic nor icteric. The thyroid gland was not palpable. The lungs were clear and cardiac sounds were normal with auscultation. The abdomen was flat and not tender. The bowel sounds were normal. There was no edema in the extremities. She refused to take a MMSE (Mini Mental Status Examination).

Laboratory data and imaging studies at hospitalization: The blood levels of albumin was 3.5 g/dL (low), AST 24 U/L, ALT 18 U/L, total bilirubin 1.2 mg/dL, ALP 465 U/L (high), gamma-GTP 29 U/L, CPK 35 U/L (low), BUN 4.5 mg/dL (low), creatinine 0.35 mg/dL, Na 139 mEq/L, Cl 95 mEq/L (low), K 3.9 mEq/L, Ca 9.0 mg/dL, Fe 34 µg/dL, total cholesterol 238 mg/dL (high), LDL 141 mg/dL (high), HDL 79 mg/dL, TG 89 mg/dL, FBS 101 mg/dL, HbA1c 5.9%, CRP 1.29 mg/dL (high), WBC 7300/µL, RBC 366 ×10<sup>4</sup>/µL (low), Hb 11.5 g/dL, Ht 35.5%, Plt 33.4 ×10<sup>4</sup>/µL, MCV 97 fL, MCH 31.4 pg, MCHC 32.4%, TSH 4.78 µIU/mL (high), free T3 2.3 pg/mL, free T4 1.1 ng/dL, Vitamin B12 441 pg/mL,

folate 7.5 ng/mL, HBs Ag <8, RPR (-), HCV Ab (-). Urinalysis was unremarkable. Chest x-ray was unremarkable. EKG showed first AV block. CT scan of the head was normal. EEG had no abnormal findings.

Course during hospitalization: The water intake was restricted to 2 liters per day. Quetiapine 25 mg orally twice a day was added to her previous prescription (magnesium oxide 250 mg orally three times a day, lansoprazole 15 mg orally once a day, alfacalcidol 0.5  $\mu$ g orally once a day, brotizolam 0.25 mg orally once a day at bed time). However, her urge to water intake was not reduced. In addition, sertraline 25 mg orally was administered for anxiety. The sodium level in the blood went down to 125 mEq/L. The level of Na in the urine was 16 mEq/L and the urine osmolality was 158 mOsm/kg H<sub>2</sub>O. We suspected the patient was drinking tap water in her bathroom and stopped the water supply. Her sodium level gradually normalized. Alendronate 35 mg orally a week and calcium L-aspartate hydrate 200 mg orally twice a day were supplied because of osteoporosis. Since ALP level was increased to 505 U/L, the fraction was analyzed. ALP1 was 24.7 U/L (high), ALP2 274.2 U/L (high), ALP3 134.8 U/L, and ALP4 71.2 U/L. AST, ALT, gamma GTP, bilirubin was within the normal limits. The liver was normal with the abdominal CT scan. Therefore, mild drug-induced liver damage was suspected. She was still complaining about her thirst. Sertraline was replaced with mirtazapine 15 mg orally once a day at bed time to increase her appetite. Although risperidone 0.5 mg orally twice a day and irbesartan 25 mg orally once a day was tried to take place of quetiapine, her thirst was not controlled with them. Risperidone and irbesartan was gradually reduced and stopped, and then olanzapine 5 mg orally a day was prescribed. However, it was gradually tapered since

her urge toward water intake was unabated. Tsumura (34) 3 g orally three times was tried to reduce her thirst. But she refused to take it because she disliked the taste. Since we do not have a facility to use clozapine, off-label use of topiramate was considered because it has been reported that it reduced urges like appetite and alcohol craving<sup>21,22</sup>.

Administration of topiramate was started at 25 mg orally once a day and then 25 mg was increased every week up to 100 mg twice a day. Since topiramate is not allowed to be prescribed as a monotherapy in Japan, a small amount of valproate (100 mg orally once a day) was added. Her excessive thirst was gradually reduced. Surprisingly ALP level was reduced to 358 U/L and CRP level was decreased within the normal limit when she was discharged on April 26<sup>th</sup>, 2017. Follow-up continues as an outpatient at our facility. She gained weight from 28.6 kg at hospitalization and weighed 37.5 kg on Dec. 21<sup>st</sup>, 2017. Her husband reported that she no longer woke him up at night to force him to bring water to her. He said that now he has good sleep at night.

## DISCUSSION

It is well known that some schizophrenia patients on antipsychotics demonstrate primary polydipsia. The antipsychotics cause oral dryness as a side effect. However, not all patients have excessive water intake enough to cause hyponatremia. It is presumed that a central defect in thirst regulation plays a role in the pathogenesis of polydipsia<sup>4,24</sup>. In some cases, for example, the osmotic threshold for thirst is reduced below the threshold for the release of ADH<sup>25</sup>. In contrast to normal subjects in whom the thirst threshold is roughly equal to or a few mOsm/kg H<sub>2</sub>O higher than the threshold for ADH<sup>26</sup>, these patients will continue to drink until the

plasma osmolality is less than the threshold level. This may be difficult to achieve, however, since ADH secretion will be suppressed by the fall in plasma osmolality, resulting in rapid excretion of the excess water and continued stimulation of thirst. The mechanism responsible for abnormal thirst regulation in patients with primary polydipsia is unclear. Since this patient refused to eat enough, she could have had anorexia nervosa. Increased liquid consumption may compensate for low food intake and to decrease the sensation of hunger<sup>27</sup>.

Until now some medical treatments have been reported. I attempted to treat my patient with a few antipsychotics, antidepressants, and an angiotensin II receptor blocker as described before<sup>14,15</sup>. However, they all failed. The possible explanation could be because the patient does not have psychosis, anxiety, or abnormal regulation of the angiotensin system. A trial with topiramate was suggested to suppress her excessive thirst because it is reported effective for excessive eating and addictive behaviors<sup>21,22</sup>. Furthermore a report was found that topiramate was used successfully for the treatment of schizophrenia with polydipsia resulting in hyponatremia<sup>23</sup>. Fortunately it is working for the patient. Although the exact mechanism is not known, topiramate may work on the glutamatergic system in the nucleus accumbens which has a significant role in the cognitive processing of aversion, motivation, reward, and reinforcement learning; hence, it has a significant role in addiction<sup>28</sup>. In addition, topiramate is used for my patients with schizophrenia who have excessive water intake with or without hyponatremia. So far the trials are all working. One patient was transferred from the closed ward to the open ward in our hospital because he no longer had the urge to keep drinking. Refractory primary polydipsia behavior requires long-term hospital-

ization with inhumane means like seclusion and restraints. Long-term hospitalization could cause financial burden in the healthcare system as well. This report demonstrates that topiramate may become an option for patients that have failed other medical approaches.

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