中文題目：與 DDAVP 和 mirtazapine 治療相關的急性低鈉血症
英文題目：Acute hyponatremia associated with DDAVP and mirtazapine treatment
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Case Presentation

A 51-year-old man was admitted to hospital because of seizure attack and hyponatremia after taking desmopressin before sleep for three times. He had the medical history of major depressive disorder with daily mirtazapine 30mg for two and a half years and hypertension with daily valsartan 40mg and bisoprolol 1.25mg for 3 years. Three months before admission, he felt urinary frequency, nocturia, and have to strain to begin urination. Urologic studies revealed an enlarged prostate gland (33.6 ml) by echography, kissing lateral lobes of prostate gland by cystoscopy and normal serum level of prostate specific antigen (1.65 ng/ml). Due to few response to medication treatment, he received transurethral resection of prostate gland one month before admission. Three days before admission, he came to urologic clinic for post-operative follow-up, and still complained of urinary frequency and nocturia even after the operation. Therefore, the urologist prescribed oral desmopressin 0.05 mg before sleep for the symptom of nocturia. After starting desmopressin treatment, his blood pressure increased and insomnia progressed. Unfortunately, He had a seizure attack and loss of consciousness for few minutes on the third day after desmopressin treatment.

At emergency department, his wife stated he usually felts thirsty sensation and needed to drink about 8-10 L of water every day owing to the side effect of mirtazapine. He felt decreased urine amount, insomnia and agitation in the past two days after taking desmopressin. On physical examination, vital sign and neurologic exanimation showed body temperature 37.0°C, heart rate 60 beats/min, respiratory rate 16 breaths/min, blood pressure 154/119 mmHg, and Glasgow coma scale E2V3M4 without significant focal neurologic signs. Laboratory data of serum revealed sodium 109 mmol/L (sodium 141 mmol/L one month ago), potassium 3.2 mmol/L, creatinine 0.75 mg/dL, urea nitrogen 5 mg/dl, and glucose 159 mg/dl. Urine biochemistry showed sodium 49 mmol/l, creatinine 25.6 mg/dl, and osmolality 188 mOsm/kg. His urine toxic screen also revealed positive benzodiazepine. Brain computed tomography revealed only mild focal demyelination. He was admitted to intensive care unit under the impression of acute hyponatremia associated with desmopressin and mirtazapine treatment. We closely monitored his serum sodium level every four hours to prevent the development of neurologic sequelae during rapid sodium correction (Figure 1). On the second day of hospitalization, alert consciousness and stable blood pressure (117/69 mmHg) returned. Further electroencephalography did not show any spike wave. The psychiatrist prescribed agomelatine instead of mirtazapine for further treatment of major depressive disorder and educated the patient to prevent polydipsia.

Discussion

Severe hyponatremia, defined as serum sodium level <125 mmol/L, is a life-threatening disease with the prevalence to be 0.6% and the mortality to be 8.5% (serum sodium level 120-124 mmol/L) and 6.7% (serum sodium level <120 mmol/L). The symptoms of severe acute hyponatremia present for less than 48 hours, including nausea, vomiting, altered mental status, seizures, coma, and death. Acute hyponatremia most often results from psychogenic polydipsia or 3,4-methylenedioxy-N-methamphetamine (ecstasy) use. Several drugs, such as diuretics, antiepileptic drugs and antidepressants, can also induce hyponatremia, but the onset of symptoms is usually more than 48 hours. In a research of 2,233 identified reports using information reported to the US Food and Drug Administration Adverse Event Reporting System showed that the adjusted reporting odds ratio for the association between

antidepressant drug use and hyponatremia was 1.91 (95% confidence interval 1.83-2.00). Mirtazapine, a serotonin receptor blocker, had the strongest association, followed by selective serotonin reuptake inhibitors. In this case, he had been taken daily mirtazapine 30mg for two and a half years and his serum sodium was 141 mmol/L one month ago before this admission. We favored that the acute hyponatremia might result from polydipsia (mirtazapine-induced thirsty sensation) and desmopressin treatment.

Desmopressin, approved by US Food and Drug Administration for the treatment of nocturnal polyuria, increases urine osmolality and decreases urine volume. In a double-blind placebo-controlled study, the onset of hyponatremia (<130 mmol/L) was usually more than 48 hours and incidence was 4%. However, desmopressin should not be prescribed in patients with primary polydipsia or psychogenic polydipsia induced-polyuria (40 ml/kg/24 h) to prevent to the development of fluid retention and hyponatremia. In this case, he drank water 8-10 L/day, which could cause polyuria at night and be misdiagnosed as nocturnal polyuria if not taking detailed history of water intake amount.

Treatment of drug-induced symptomatic hyponatremia includes the assurance of discontinuation of inducing agents, avoidance of readministration, and hypertonic saline (3% sodium chloride). Nevertheless, in a study of desmopressin-associated hyponatremia and brain damage, discontinuing desmopressin was reported to lead to rapid correction of the serum sodium and resultant severe neurological injury. The difficulty of treating these patients is the shift of initially anti-diuretic state to a state of water diuresis after discontinued the desmopressin. In this case, we withdrew desmopressin after hospitalization and closely monitored serum sodium level. There was no neurologic sequela noted during the treatment course.

In conclusion, this case warns us that using desmopressin for the treatment of nocturia polyuria should evaluate 24 hours urine amount first to exclude polydipsia-related polyuria, especially in the psychologic patients with antidepressants, start with low dose desmopressin, monitor serum sodium level in the first week and first month, and educate patient water restriction and the symptoms of hyponatremia.

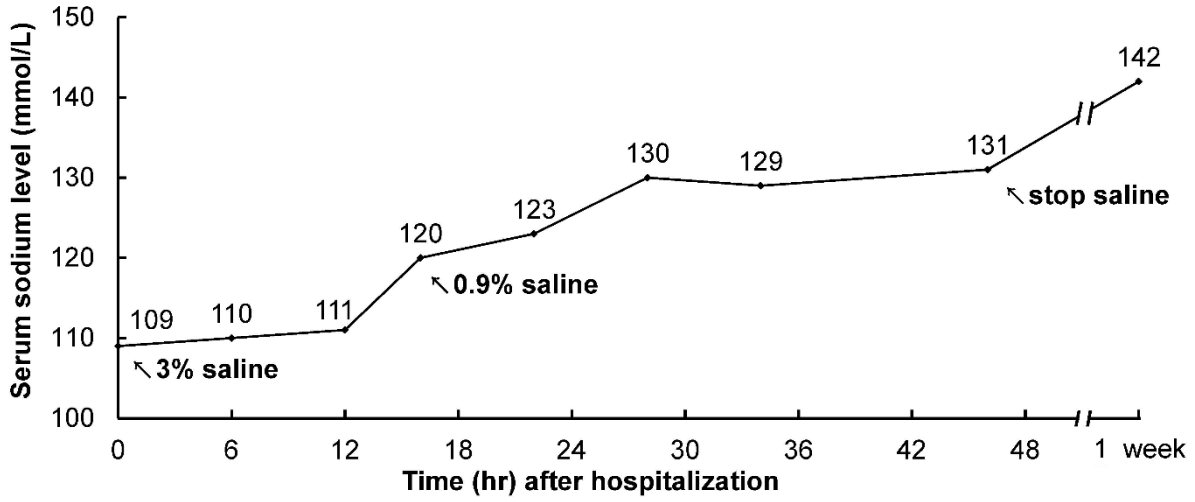

Figure 1. Serum sodium levels during the treatment course of hospitalization.