PERIOPERATIVE MANAGEMENT OF A PATIENT WITH SYNDROME OF INAPPROPRİATE SECRETION OF ANTIDIURETIC HORMONE: CONTRIBUTION OF TOLVAPTAN

Case Report

UYGUNSUZ ADH SENDROMU OLAN HASTANIN PERİOPERATİF YÖNETİMİ: TOLVAPTAN'IN KATKISI

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SUMMARY

The treatment of SIADH, consists of fluid restriction, salt or salt plus a loop diuretic administration, which may be poorly complied by the patients. In this case we report successfull management of a patient with rezistant(resistant) hyponatremia due to cranial meningioma with oral vasopressin receptor antagonist (Tolvaptan) therapy.

Key words: *Tolvaptan; Inappropriate ADH Syndrome; craniotomy; hyponatremia.*

ÖZET

Uygunsuz ADH sendromunun tedavisi, genellikle hastalar tarafından güç uyum sağlanan, sıvı kısıtlaması, tuz ilavesi ya da tuz tedavisine ek olarak verilen "loop" diüretiğiyle yapılır. Bu olguda, kranial menenjioma bağlı dirençli hiponatremi tablosu gelişen hastanın oral vazopressin antagonisti Tolvaptan ile başarılı tedavisini paylaşmaktayız.

Anahtar kelimeler: *Tolvaptan; uygunsuz ADH sendromu; kraniotomi; hiponatremi.*

INTRODUCTION

Hyponatremia has been reported to be 1–15% in hospitalized patients and associated with a mortality rate from 7 to 60% (1). Hyponatremia is more common in neurologic diseases and associated with 1.5 fold higher in-hospital mortality than in the other hospitalized population (2). The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is one of the most common causes of hyponatremia and results from nonosmotic release of vasopressin from the pituitary gland or from an extracranial ectopic tumoral tissue secretion (3).

The treatment of SIADH, consists of fluid restriction, salt or salt plus a loop diuretic administration, which may be poorly complied by the patients. Furthermore, this treatment may not work

in some cases. The recent introduction of vasopressin receptor antagonists considerably improved the unconvincing results of the conventional treatment. The following case report illustrates the successful management of a patient with hyponatremia and SIADH due to cranial meningioma of the left cavernous sinus with oral vasopressin receptor antagonist (Tolvaptan) therapy.

CASE REPORT

A 77-year-old woman was referred to our Neurosurgery clinic for the management of an intracranial tumor invasing the left cavernous sinus, detected after ptosis of the left eyelid two weeks ago. She had a medical history of hypertension, cerebrovascular accident, severe carotid artery disease and two episodes of hyponatremia (one symptomatic seven months ago and one asyptomatic two months ago). Despite extensive research at that time, the etiology of hyponatremia remained uncertain. The patient's medications included Losartan, clopidogrel, acetylsalicylic acid, and carbamazepine, dexamethasone started two weeks ago. At physical examination blood pressure was 126/68 mmHg, with regular pulse of 74 bpm and she did not have apparent sings of edema or dehydration. Magnetic resonance imaging revealed a brain tumor which was suspected to be metastatic and compressing both hypophysis gland and hypothalamus. However, the results of computed tomography and FDG-PET/CT ruled out this possibility. The cranial MRI evaluation performed 8 months ago was normal. Her serum sodium was 128 mmol/L and potassium was 3.3 mmol/L. Laboratory data were as follows: serum osmolality: 277 mOsm/kg H_2O, urinary osmolality: 597 mOsm/kg H2O urinary sodium: 97.1 mmol/L, normal adrenal and thyroid functions. Therefore, SIADH which might be related to carbamazepine use were(was) considered as the most likely diagnosis. Despite discontinuation of carbamazepine, aggressive fluid restriction (1000 mL/day) and oral salt tablets, the patient's serum sodium level was varied between 130 and 134 mmol/L for one week and decreased to 128 mmol/L at the day of operation. Surgery was postponed because of the risk of intraoperative cerebral edema. In this case, the contribution of the tumor itself on SIADH was considered. Therefore, therapy with 15 mg Tolvaptan was decided. Serum sodium was measured every 4 hours, on the second day of the therapy, serum sodium reached to 132 mmol/L. Treatment was continued with 30 mg tolvaptan for 4 more days, serum sodium stabilized between 134-138 mmol/l and she underwent a successful craniotomy which ended up with near total removal of the tumor. At the end of the surgery the patient woke up uneventfully and transferred to the intensive care unit. Histopathologic examination revealed a grade 2 meningioma.

DISCUSSION

SIADH is the most frequent cause of hyponatremia and results from nonosmotic release of vasopressin (1). Criteria for the diagnosis of SIADH includes hyponatremia, hypoosmolality, a (an) urine osmolality above 100 mosmol/kg, a (an) urine sodium concentration above 40 mEq/L, normal adrenal and thyroid gland functions, clinical euvolemia and no recent use of a diuretic agent (3). The causes of SIADH are numerous and as follows; malignant diseases, pulmonary and central nervous system diseases, and drugs that can stimulate the release of ADH or potentiate its actions (4). Based on these criteria, the cause of hyponatremia was diagnosed as SIADH related to meningeoma(meningioma) which was not reported before.

The risk of hyponatremia and neurologic complications rises with increasing age and (in) female gender (5). Hyponatremia leads to cerebral edema due to low serum osmolality. The restoration of the brain volume occurs through the adaptation mechanisms of brain cell, also known as

''osmoregulation'', by losing the electrolytes and organic osmolytes (6). Patients with neurologic diseases may be more vulnerable to cerebral edema due to impaired osmoregulation in pathologic lesions of the brain. Thus, these patients can exhibit more aggressive cerebral edema with deterioration of both clinical status and intracranial pressure than hyponatremic patients without brain lesions. In addition, hyponatremia accompanied by central nervous system (CNS) disorders actually has (was) shown to increase delayed cerebral ischemia and mortality rates (7). In our patient, conventional treatments for SIADH was failed and surgery was postponed because of the increased risk of intraoperative cerebral edema.

There are no professional guidelines for treating SIADH. The recent introduction of vasopressin receptor antagonists considerably improved the unconvincing results of conventional treatment consisting of fluid restriction, salt supplementation or salt tablets plus loop diuretic. The vasopressin receptor antagonists produce a selective water diuresis (aquaresis) without affecting sodium and potassium excretion (8). Ensuing the loss of electrolyte-free water will tend to raise the serum sodium in patients with SIADH and may improve mental status in patients with a serum sodium lower than 130 meq/L. There are three kind of receptors for vasopressin (ADH): the V1a, V1b, and V2 receptors. The V2 receptors primarily mediate the antidiuretic response, while V1a and V1b receptors principally cause vasoconstriction and mediate adrenocorticotropin release, respectively. Oral tolvaptan, approved by the FDA in 2009, is selective for the V2 receptor, while an intravenous agent conivaptan, blocks both the V2 and V1a receptors. Two major potential adverse effects of oral V2 receptor antagonists are, increased thirst, which may limit the rise in serum sodium and rapid correction of the hyponatremia, which can lead to irreversible neurologic injury (9). However, recent recommendations have suggested a maximum rate of correction of less than 10 meq/L in the first 24 hours in hyponatremic patients. Because of the risk of neurologic injury, hospitalization and close monitorization of the serum sodium levels is required at the the beginning of therapy. We followed serum sodium levels every four hours during first day of therapy and continued with daily follow-up. With 30 mg tolvaptan, the serum sodium level was kept between 134-138 mmol/l and she underwent surgery without any complications.

In this case we reported the successful treatment of a resistant SIADH case related to meningioma with Tolvaptan.

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