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Syndrome of inappropriate antidiuretic hormone secretion in a patient with advanced bladder cancer

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ABSTRACT

A 57-year-old male patient was admitted to the hospital because of macroscopic hematuria. He was diagnosed as transitional cell carcinoma of the bladder. A transurethral resection of the tumor was followed by a radical cystoprostatectomy. Two months post-operatively, he was admitted to the hospital because of severe lumbar and leg pain and on the radiologic evaluation bone, right suprarenal, lung metastases and multiple abdominal lymphadenopathies were found. Meanwhile, a hyponatremia was observed and was corrected with water restriction. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) was diagnosed in the absence of other causes of hyponatremia [Turk J Cancer 2007;37(2):69-71]

KEY WORDS:

Inappropriate ADH secretion, bladder cancer, progression

INTRODUCTION

Hyponatremia is not uncommon in cancer patients and syndrome of inappropriate antidiuretic hormone secretion (SIADH) is one of the leading causes. Neurological defects and serious sequelae can complicate severe hyponatremia and these can be prevented by early diagnosis and adequate measures. Here we present a 57-year old male patient with the diagnosis of transitional cell carcinoma of the bladder which was complicated with SIADH at recurrence.

CASE REPORT

A 57-year-old patient was admitted to the hospital because of macroscopic hematuria. The cystoscopic evaluation found a vegetating bladder mass. The biopsy material provided a histopathological diagnosis of transitional cell bladder carcinoma. A transurethral resection was performed and further therapy was not proposed to the patient. Eight months later, he was readmitted to the hospital because of the reappearance of hematuria. Pelvic ultrasonography found a 2 cm lobulated mass at the lateral and a 3 cm mass at the posterior wall of the bladder. A more extensive surgical intervention consisting of radical cystoprostatectomy and bilateral lymph node dissection with ileal loop-urinary loop diversion was performed. The histopathological evaluation showed the transitional bladder carcinoma same as initial diagnosis. It was invading the vascular and superficial muscle layers (pT2a, N0). Adjuvant treatment

was not proposed.

Two months after the surgery, the patient visited the hospital because of lumbar and leg pain. The physical examination revealed pain when pressure was applied to lumbar vertebrae and a sciatic pain. He was admitted to the hospital. On his radiologic evaluation, the CT scan showed bone, right suprarenal and lung metastases as well as multiple intraabdominal lymph nodes. Also asymptomatic hyponatremia was observed on his blood biochemistry examination. The serum sodium level was 125 mMol/L while it was previously within the normal limits. Other parameters of the blood biochemistry and blood counts were normal. A systemic evaluation of the patient did not reveal clinical syndromes such as vomiting or diarrhea which could cause a gastrointestinal loss, nor a history of use of any medication such as diuretics which could influence changes in the Na+ level. He was euvolemic in clinical examination. Spot urine analysis was normal with a density of 1.015 and sodium level of 70 mMol/L. The urine osmolality was higher than blood osmolality being 258 mOsm/kg and 367 mOsm/kg H_2O, respectively. The thyroid function tests were within normal limits. An ACTH stimulation test was performed to rule out adrenal insufficiency and the cortisol level was able to increase adequately. No infection was found. Cranial and hypophysis MRI scans were normal. After all these procedures, SIADH was considered to be the cause of persisting hyponatremia after ruling out all other possibilities. An 800 ml/day water restriction was performed and the serum sodium was observed to rise to 132 mMol/L.

The patient was put on a chronic water restriction diet with 1-1.5 L of oral water intake per day. A chemotherapy regimen consisting of 3 weekly cycles of carboplatin AUC 5 on day 1 and gemcitabine 1250 mg/m^2 on day 1 and 8 was started for his metastatic cancer. Six cycles were completed with some delay due to recurrent urinary infections. His disease remained stable during the treatment and the pain was controlled with low doses of fentanyl patches. The serum sodium level remained within normal limits at the follow-up except for one occasion. At the completion of the chemotherapy, the patient tried voluntarily to stop the water restriction and the somnolence recurred when the sodium level decreased to 124 mMol/L. This was corrected easily with the return to water restriction.

His tumoral disease was stable at the end of chemotherapy. He was on supportive care after the chemotherapy. He did not receive further chemotherapy because of persisting hematologic toxicity. He was dead four months later because of rapid progression of his cancer.

DISCUSSION

A 57- year old male patient was treated surgically for transitional cell carcinoma of the bladder. A symptomatic hyponatremia was observed when he was admitted for early recurrence of his cancer with systemic metastases. SIADH was considered as the cause of the hyponatremia after ruling out other possibilities. A normalization of the serum sodium level at the end of water restriction confirmed the diagnosis of SIADH. The SIADH of the patient was considered paraneoplastic, i.e. secondary to his tumor because it accompanied the progression of the disease.

SIADH was first described by Schwartz et al. (1), in two patients with bronchogenic carcinoma of the lung. Since that time it has been realized as the etiology of most hyponatremic cases observed in cancer patients.

Essential diagnostic criteria for SIADH are reduced effective extracellular volume osmolality (Plasma osmolality <275 mOsm/kg H_2O); inappropriate urine concentration (Urine osmolality >100 mOsm/kg H_2O) in the presence of normal renal function; euvolemia; increased sodium excretion; exclusion of any other potential conditions which can cause euvolemic hypoosmolality such as hypothyroidism, hypocortisolism and diuretic use. Water restriction test is not essential for the diagnosis. However it can provide supporting information (2).

All the above mentioned criteria were met by the patient and the water restriction confirmed the diagnosis of SIADH. SIADH can be induced by various pulmonary and central nervous system diseases or it can be caused by ectopic secretion of ADH by tumors. Small cell lung cancer is the most frequent cause of paraneoplastic SIADH. SIADH was also reported with pancreatic carcinomas and rarely with other cancers such as neuroblastoma and lymphoma.

To our knowledge, only one case of SIADH related to the bladder cancer was reported in the literature (3). In this report, SIADH was diagnosed twenty months prior to the emergence of bladder cancer and as an early finding.

However, in our case, hyponatremia was not observed during the initial diagnosis and it appeared when the tumor recurred with systemic metastases. Our report has some similarities with the case of Andersen and Sorensen (4), who observed the appearance of SIADH during disease progression in a patient with breast cancer.

We can hypothesize that the SIADH in our patient is secondary to an ectopic ADH secretion and it reached significant levels with clinical consequences following an increase of the tumor mass. The systemic chemotherapy failed to decrease the tumor mass as well as to correct the SIADH. A simple measure such as chronic water restriction was able to maintain the serum sodium within normal levels.

The SIADH can be frequently observed in neoplasms such as bladder or other cancers, but missed often because of complicated clinical situations of patients with extensive metastatic diseases. Serum electrolytes should be evaluated carefully in such patients, because a simple hyponatremia can alert on the possibility of SIADH which can cause some neurologic damages in the absence of adequate treatment or with rapid correction of the hyponatremia.

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