A report on the syndrome of inappropriate anti-diuretic hormone secretion associated with multiple myeloma

Ran Tang, Jia-Jia Zhang, Yu-Ping Zhong

Department of Hematology, Beijing Chao-Yang Hospital (West), Capital Medical University, Beijing 100043, China.

To the Editor: Hyponatremia, defined as a serum sodium concentration <135 mmol/L, is the most common water-electrolyte imbalance in clinical practice. Hyponatremia can be a complication of other diseases (eg, heart failure, renal failure, pneumonia). Hyponatremia can be divided into three main classes: hypovolemic; euvolemic, hyper- and hypervolemic. The pathogenesis of hyponatremia including taking drugs such as water pills (diuretics) and some anti-depressants and pain medications; heart failure and kidney or liver disease, bouts of chronic, severe diarrhea or vomiting.

Syndrome of inappropriate anti-diuretic hormone (SIADH) is a hormone imbalance disease that can retain water. SIADH can be a significant cause of cancer-related hyponatremia, but relatively rare in hematologic disease. Here, we report SIADH in a multiple myeloma patient.

A 60-year-old Chinese man was admitted to our department with weak in the legs that was discovered 3 months earlier. Accompanied by numbness of lower limbs, skin tingling sensation of lower limbs, numbness. The symptoms become worse, with walking difficulty for 10 days. He had a history of hypertension. He lost 10 kg in 3 months. Physical examination: the patient had clear consciousness, indifferent expression, normal muscle strength, and sensation of lower limbs. Laboratory results: hemoglobin 130 g/L, albumin 38 g/L, globulin 45 g/L, creatinine 52.9 μmol/L, sodium 111.9 mmol/L (normal range: 135–145 mmol/L), calcium 2.21 mmol/L, β2-microglobulin was 2.27 mg/L. Immunoglobulin (Ig) G was elevated to 4.13 g/L (normal range: 0.87–1.70 g/L) with suppressed levels of IgM, 0.013 g/L (normal range: 0.035–0.220 g/L) and IgA, 0.033 g/L (normal range: 0.011–0.410 g/L). Protein electrophoresis showed a monoclonal peak, the M component is 23%. Immunoelectrophoresis of serum proteins showed an IgG kappa M-protein. Bone marrow examination revealed that 23% of nucleated cells were myeloma cells with unbalanced κ - and λ-type Ig. Bone marrow biopsy with the immunohistochemical study of the abnormal cells demonstrated a lack of expression of B- and T-cell markers but strong expression of CD38 and CD138, cytoplasmic IgG and cytoplasmic kappa. The low dose computed tomography showed that bone lesions and lytic at the thoracic and lumbar spine. Patient has normal chromosomes by fluorescence in situ hybridization. We diagnosed the patients with IgG-κ type of multiple myeloma, stage III (Durie-Salmon Staging System), stage I disease (International Staging System).[1]

We reviewed his serum sodium level 114 mmol/L and showed a plasma osmolality of 228.0 mOsm/kg per H2O (normal range, 285–295 mOsm/kg per H2O), while urine sodium level was 117.9 mmol/mL, urine-osmolality was 261.9 mOsm/kg per H2O. Urine sodium was 400.9 mmol/24 h (normal range: 40–220 mmol/24 h). Thyroid function and adrenal cortical function was normal. Magnetic resonance imaging examination of the sellar region of the pituitary revealed that the upper margin of the pituitary was flat with a diameter of 0.7 cm, and the lower part of the hypophysis after enhancement showed a reduced focal enhancement with a diameter of about 0.3 cm, considering a pituitary adenoma [Figure 1]. A diagnosis of SIADH secretion was made. Fluid restriction and an oral dose of Samsca (Otsuka Co., Ltd, Lin-an, Zhejiang, China) made his sodium levels increased to normal.

For myeloma, the patient was treated with bortezomib (Xi’an Janssen Pharmaceutical Ltd., Xi’an, Shaanxi, China) (1.3 mg/m² on days 1, 4, 8, and 11) and methylprednisolone (80 mg on days 1, 4, 8, and 11; Pfizer Inc., New York, NY, USA). After two cycles, the level of IgG decreased from 4.130 to 1.140 g/L. Following the treatment of multiple myeloma, and the patient achieved complete remission (CR). The patient gradually stopped using Samsca (Otsuka Co., Ltd), and the sodium level remained normal. At present, the patient was followed up for 2 years the disease is still in CR, blood sodium is normal.
Only a few cases of SIADH have been reported in patients with multiple myeloma associated with the use of bortezomib and cyclophosphamide.[2-5] SIADH is rare as the first symptom in myeloma patients. The mechanism is not entirely clear. For most tumor-related SIADH, the cause is excessive release of anti-diuretic hormone (ADH) into the blood by tumor tissue. However, some studies have shown that sometimes ADH cannot be detected in the tumor tissue, indicating that part of neoplastic SIADH is not caused by ADH generated with the tumor, and such SIADH essentially belongs to the ectopic endocrine syndrome. The mechanism of such SIADH may be as follows: (1) tumor tissues produce some ADH-like substances; (2) the tumor tissue produces certain mediators to stimulate the secretion of pituitary ADH; for the tumor-related SIADH, treatment of primary diseases is crucial and then limit intake of water.

Although the patient had a pituitary adenoma, it was not be treated and the serum sodium returned to normal, so we considered that SIADH in the patient was irrelevant. We treated our patient with fluid intake restriction and the oral administration of additional Samsca (Otsuka Co., Ltd), but his recovery was delayed. With the remission of multiple myeloma, hyponatremia is well controlled. The hyponatremia gradually disappeared.

In summary, SIADH as the first symptom is rare in myeloma patients. Improving the understanding of SIADH and actively treat the myeloma, patients may be cured.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient provided his consent for the images and other clinical information to be reported in the journal. The patient understands that her names and initials will not be published and efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Funding**

This study was supported by a grant from the Beijing Natural Science Foundation (No. 7162067).

**Conflicts of interest**

None

**References**

1. Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol 2014;15:e538–e548. doi: 10.1016/S1470-2045(14)70442-5.

2. Lv CL, Li J. Bortezomib as a probable cause of the syndrome of inappropriate anti-diuretic hormone secretion: a case report and review of the literature. Mol Clin Oncol 2017;7:667–672. doi: 10.3892/mco.2017.1366.

3. Abraham A, Shafi F, Iqbal M, Kollipara R, Rouf E. Syndrome of inappropriate antidiuretic hormone due to multiple myeloma. Mo Med 2011;108:377–379.

4. Nakayama-khiyama S, Yokote T, Iwaki K, Takubo T, Tsuji M, Hanafusa T. Syndrome of inappropriate antidiuretic hormone secretion associated with plasma cell myeloma. Br J Haematol 2011;152:125. doi: 10.1111/j.1365-2457.2010.08462.x.

5. Björck E, Samuelsson J. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) after treatment with cyclophosphamide, alpha-interferon and betamethasone in a patient with multiple myeloma. Eur J Haematol 1996;56:323–325. doi: 10.1111/j.1600-0609.1996.tb00724.x.

**How to cite this article:** Tang R, Zhang JJ, Zhong YP. The first syndrome of inappropriate anti-diuretic hormone secretion case report associated with multiple myeloma. Chin Med J 2020;133:1493–1494. doi: 10.1097/ CM9.0000000000000837