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LETTER TO THE EDITOR

Syndrome of inappropriate antidiuretic hormone secretion in a patient with castration-resistant prostate cancer treated with enzalutamide

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To the Editor,

Enzalutamide is approved by FDA for the treatment of castration-resistant prostate cancer (CRPC) [1]. Common adverse events include fatigue, diarrhea, and hot flashes [1]. However, syndrome of inappropriate antidiuretic hormone secretion (SIADH) is not described in the drug's prescribing information, and has not been previously reported. We report an initial case of enzalutamide-induced SIADH.

An 86-year-old male with CRPC presented to the emergency department with nausea, vomiting and tremor of his hand. He was previously diagnosed with prostate cancer and was receiving anti-androgen medicines and luteinizing hormone-releasing hormone agonists. However, because of increasingly elevated PSA, he was diagnosed with CRPC and had started treatment with enzalutamide three weeks earlier. At examination, his consciousness was clear, blood pressure was 164/94 mmHg, heart rate was 89 beats/min, and he appeared euvolemic. Laboratory investigation revealed a low serum sodium concentration (115 mmol/l), high urine sodium concentration (62.2 mmol/l), low serum osmolality (244 mOsm/l), high urine osmolality (348 mOsm/l), and an elevated plasma arginine vasopressin concentration (AVP, 7.0 pg/ml). Both low blood urea nitrogen (10.0 mg/dl) and low plasma uric acid (3.0 mg/dl) suggested SIADH. Other laboratory findings, including serum potassium and blood glucose concentrations, were within normal ranges. Furthermore, renal, thyroid, and adrenal function tests were normal. Brain magnetic resonance imaging and whole-body contrast-enhanced computed tomography revealed no specific abnormalities, including no evidence of metastasis. The patient was not taking any diuretic agents, and no other medications had been prescribed before or after initiating enzalutamide. The patient was diagnosed with SIADH, enzalutamide use was discontinued, and he was treated with fluid restriction. Ten days after enzalutamide discontinuation, his symptoms had fully resolved, with both serum sodium concentration and plasma AVP level returning to normal values of 139.3 mmol/l and 2.1 pg/ml, respectively.

Hyponatremia is a common electrolyte abnormality in patients with malignancy, with SIADH as a major cause of malignancy-associated hyponatremia [2]. SIADH is characterized by impaired water excretion caused by the inability to suppress ADH secretion. There are several potential causes of SIADH, including malignant diseases, pulmonary disorders, disorders of central nervous system, and certain drugs [3].

To our knowledge, this is the first case of SIADH in a patient treated with enzalutamide. Moreover, no case of SIADH in patients treated with any other anti-androgen receptor inhibitor has been previously reported. In this case, we suspected SIADH was "probably" caused by enzalutamide [4]. First, this adverse event occurred within three weeks after receiving medication. The half-life of enzalutamide is 5.8 days; therefore, it takes few weeks to reach an effective blood concentration. Second, his SIADH symptoms resolved after enzalutamide discontinuation. Although prostate cancer can cause SIADH, it is a rare etiology of SIADH and usually involves the presence of metastatic disease.

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In addition, SIADH does not necessarily improve without the elimination of the causative factor. Enzalutamide has only been in routine clinical use for a relatively short time since its official approval, and its mechanism of action remains unclear. Therefore, clinicians should probably be aware of this serious adverse event associated with enzalutamide.

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References

[1] Scher HI, Fizazi K, Saad F, Taplin ME, Sternberg CN, Miller K, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med 2012; 367:1187–97.

[2] Castillo JJ, Vincent M, Justice E. Diagnosis and management of hyponatremia in cancer patients. Oncologist 2012;17: 756–65.

[3] Ellison DH, Berl T. Clinical practice. The syndrome of inappropriate antidiuresis. N Engl J Med 2007;356: 2064–72.

[4] Edwards IR, Biriell C. Harmonisation in pharmacovigilance. Drug Saf 1994;10:93–102.