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CASE REPORT

Syndrome of inappropriate antidiuretic hormone secretion associated with acute myeloid leukemia with multilineage dysplasia

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Abstract A patient having acute myeloid leukemia (AML) with multilineage dysplasia, developed hyponatremia and showed all symptoms of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) through a mechanism similar to tumor lysis. Retrospective immunohistochemical analysis of blast cells was positive for antidiuretic hormone (ADH) protein. According to us, this is the first case report of SIADH in an AML patient with multilineage dysplasia, showing blast cells immunostained for ADH, which clearly demonstrated that the tumor cells produced ADH.

Keywords SIADH · AML with multilineage dysplasia · ADH · Tumor lysis

Introduction

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is the most common cause of hyponatremia in hospitalized cancer patients. SIADH is characterized by increased secretion of antidiuretic hormone (ADH) that causes excessive water reabsorption in collecting ducts and results in a dilutional hyponatremia. A broad spectrum of malignant tumors has been reported to cause SIADH. A study examining large number of SIADH patients revealed that SIADH occurs in 3% of patients with head and neck cancer, 0.7% of patients with non-small-cell lung cancer, and 15% of patients with small-cell lung cancer [1].

We report a first known case of SIADH in a patient with acute myeloid leukemia (AML) with multilineage dysplasia, on initiation of chemotherapy, by demonstrating blast cells immunostained for ADH.

Case report

An 81-year-old man was admitted to the hospital for anemia and fatigue. His physical examination results were normal, except for the finding of anemic palpebrae. The results of his blood analysis were as follows: white blood cell count, 2.5×10^9/l (5.0% blast cells, 15.5% neutrophils, and 79.5% lymphocytes); red blood cell count, 144×10^{10}/l; hemoglobin count, 63 g/l; platelet count, 36×10^9/l; Na, 136 mEq/l; K, 4.0 mEq/l; lactate dehydrogenase, 261 IU/l; and C-reactive protein, 0.29 mg/dl. His plasma ADH concentration was 0.5 pg/ml (normal range, 0.3–3.5 pg/ml). Bone marrow biopsy demonstrated hypercellular marrow, and marrow aspirate showed 61.1% infiltration of abnormal cells with irregular conspicuous nuclei and fine nuclear chromatin (Fig. 1). Furthermore, smears showed pseudo-Pelger–Huet anomaly, micromegakaryocytes, and dyserythropoiesis. Dysplasia was observed in >50% of the three cell lineages. Cytochemical studies showed that most of the blast cells were positive for myeloperoxidase. Flow cytometry CD45 gating for immunophenotyping of cell

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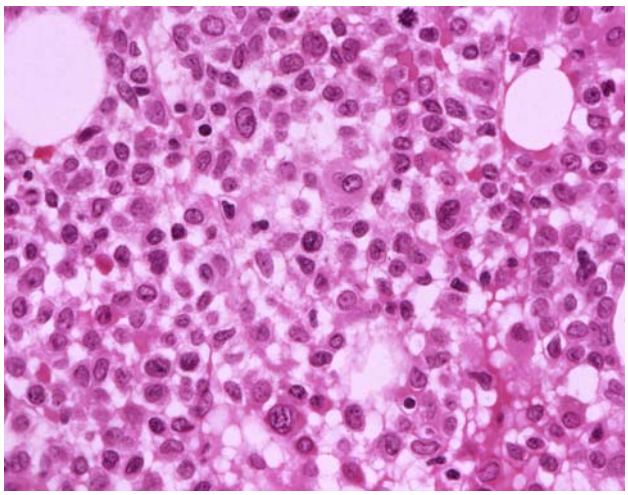

Fig. 1 Bone marrow showing abnormal cells with irregular conspicuous nuclei and fine nuclear chromatin. Original magnification, ×120

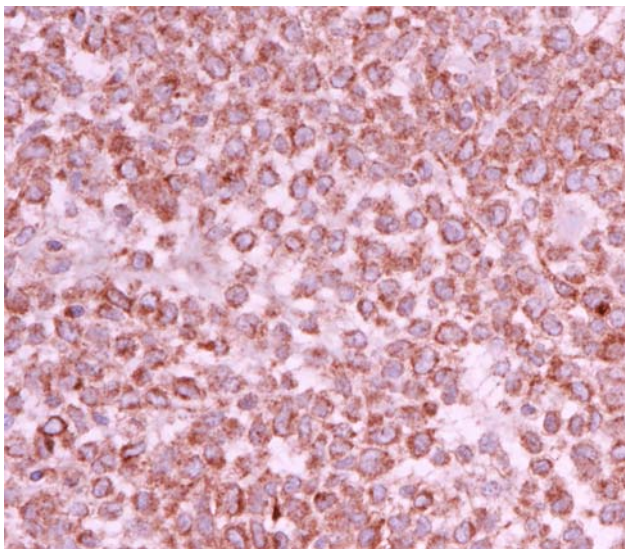

Fig. 2 Abnormal cells positive for antidiuretic hormone (ADH) protein. Original magnification, ×120

surface markers showed that most blast cells expressed CD13, CD33, and HLA-DR, but not CD56. The blast cells showed normal karyotypes with Giemsa banding. These findings indicated AML with multilineage dysplasia, as per the World Health Organization classification criteria [1].

Chemotherapy was started subcutaneously with cytarabine (20 mg/day) for 5 days, accompanied with no other previous or concomitant medication. On the 8th day of chemotherapy, the patient developed nausea and general fatigue. Findings of cranial CT scan and chest X-ray were unremarkable. The patient's serum sodium level had fallen to 127 mEq/l (below the normal range, 135–148 mEq/l), and his plasma osmolarity had decreased to 272 mOsm/kg/H_2O (below the normal range, 285–295 mOsm/kg/H_2O). On the other hand, his urine osmolarity and urinary sodium level was 547 mOsm/kg/H_2O and 52 mmol/l, respectively.

The patient's serum sodium level had decreased to 127 mEq/l and showed a plasma osmolarity of 272 mOsm/kg/H_2O, while his urine osmolarity was 547 mOsm/kg/H_2O. The patient was euvolemic and showed normal renal function tests' results. His plasma ADH concentration was 1.0 pg/ml (normal range, 0.3–3.5 pg/ml), with no evidence of thyroid, adrenal, or anterior pituitary dysfunction. The patient was diagnosed with SIADH [2] and was treated intravenously with 1000 ml 0.9% saline/day, along with restriction on fluid intake. The patient's sodium levels increased to 142 mEq/l within 3 days of treatment. However, he developed pneumonia and died during the third week of hospitalization.

Retrospective immunohistochemical analysis of blast cells was positive for ADH protein (H-300; Santa Cruz Biotechnology, Santa Cruz, CA, USA) (Fig. 2), and the case was diagnosed as SIADH that occurred through a mechanism similar to tumor lysis.

Discussion

SIADH has been reported to be associated with a number of medical conditions, including central nervous system and pulmonary disorders, and as a paraneoplastic phenomenon accompanying several malignancies. There are 4 pathways for excessive ADH secretion: ectopic ADH secretion (release by tumor tissue, infections, or conditions with altered intrathoracic pressure, such as pneumothorax or status asthmaticus) [3]; increased hypothalamic production of ADH-like substances in neurological disorders (infections, Guillain-Barré syndrome, and brain tumors) [4]; on administration of drugs (cytotoxic agents, carbamazepine, chlorpropamide, clofibrate, narcotics, sulfonylureas, etc.) [1]; and on administration of exogenous ADH [5] or oxytocine [1, 5].

The occurence of hyponatremia due to SIADH, at initial diagnosis, is a well-known paraneoplastic feature. However, SIADH has been reported to occur after the initiation of chemotherapy reflecting tumor lysis and a massive release of ADH. SIADH is most frequently associated with small-cell lung cancer, but may also occur in association with a variety of other carcinomas arising in the brain, prostate, bladder, pancreas, adrenal cortex, duodenum, head, and neck, and with mesothelioma, thymoma, sarcoma, peripheral T-cell lymphoma, anaplastic large cell lymphoma, acute myelomonocytic leukemia, and Hodgkin's disease [1, 6–15]. Although the clinical data in these studies was compatible with the diagnosis of SIADH, it was not confirmed by immunohistochemical techniques. Therefore, whether ADH had actually been produced by the tumor cells or by any other mechanism was unclear.

To the best of our knowledge, this is the first case report of SIADH in an AML patient with multilineage dysplasia showing blast cells immunostained for ADH, which clearly demonstrated that the tumor cells produced ADH.

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