

Syndrome of Inappropriate Antidiuretic Hormone Secretion in a Patient with Large Cell Neuroendocrine Carcinoma

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The syndrome of inappropriate antidiuretic hormone secretion has only been reported in a few patients with large cell neuroendocrine carcinoma (LCNEC); however, it has never been reported in a patient with LCNEC of the lung, whose serum sodium levels were normalized after surgical resection of the mass. A 63-year-old male presented with a two-day history of dizziness and recent memory loss. On admission, his serum sodium level was 113 mEq/L with a serum osmolality of 236 mosm/kg, a urine osmolality of 441 mosm/kg, and a urine sodium level of 65 mEq/L. His chest computed tomography revealed a 2.7×2.3 cm-sized mass in the left lower lobe. After surgical removal of the mass, his serum sodium concentrations were normalized, and histopathology of the mass revealed LCNEC.

Key Words: Hyponatremia, syndrome of inappropriate antidiuresis, large cell neuroendocrine carcinoma

INTRODUCTION

Since Schwartz, et al.¹ first described the syndrome of inappropriate antidiuretic hormone secretion (SIADH) in two patients with lung cancer in 1957, there have been a number of reports of SIADH in patients with malignancies.² To date, however, there were only a few reports of cases of SIADH in a patient with large cell neuroendocrine carcinoma (LCNEC). Furthermore there were no reports of a case of SIADH in a patient with LCNEC of the lung, whose serum sodium levels were normalized after surgical resection of the mass.

CASE REPORT

A 63-year-old male was admitted to our hospital because of a two-day history of dizziness, general weakness, and recent memory loss. The patient had a ten-year history of diabetes mellitus and an eight-year history of hypertension. He also had a 60 pack-year history of smoking.

Upon admission, physical examinations revealed no evidence of volume depletion, and neurologic examinations revealed no abnormalities except for slightly slurred speech. Laboratory studies showed microcytic hypochromic anemia, a blood

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urea nitrogen of 9.3 mg/dL, and a serum creatinine of 0.88 mg/dL. Urinalysis revealed trace proteinuria with no significant casts. Serum sodium concentration was 113 mEq/L with a serum osmolality of 236 mosm/kg, a urine osmolality of 441 mosm/kg, and a urine sodium concentration of 65 mEq/L. His thyroid and adrenal functions were normal. The patient denied excessive water ingestion and the usage of diuretics or any other medications affecting serum sodium levels. Based on the above information, he was diagnosed with SIADH.

No newly developed lesions in the central nervous system were found on a brain magnetic resonance imaging with angiography. An approximately 2.5 cm-sized round mass lesion on the left perihilar area was noticed on a chest X-ray, and chest computed tomography revealed a 2.7×2.3 cm-sized well-defined lobulated mass in the superior segment of the left lower lobe (Fig. 1).

The patient was initially treated with hypertonic saline

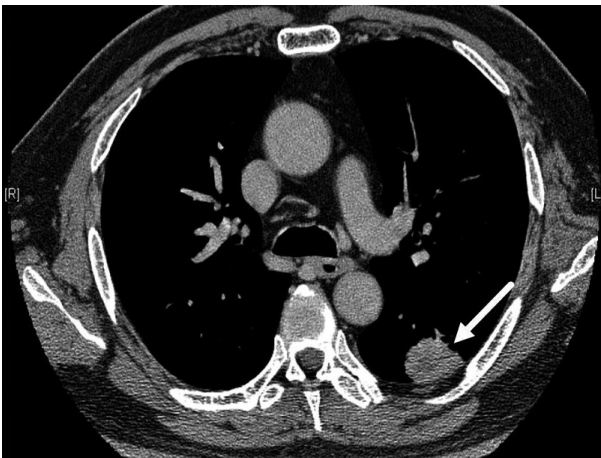


Fig. 1. Chest computed tomography revealed a 2.7×2.3 cm-sized well-defined lobulated mass in the superior segment of the left lower lobe, abutting on the parietal pleura.

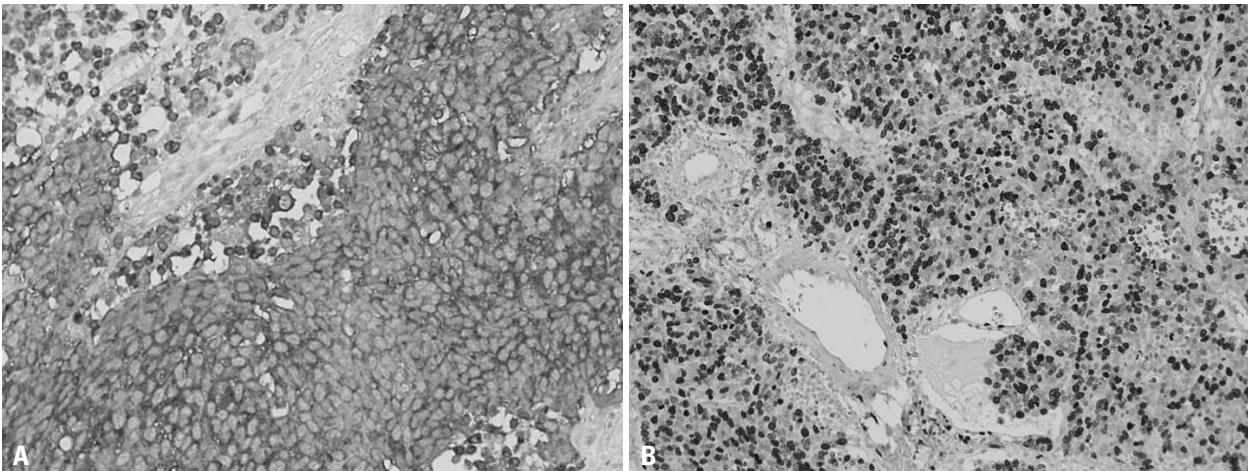


Fig. 2. Immunohistochemical staining showed diffusely strong staining for synaptophysin (A) and Ki-67 (B).

(3% NaCl: 20 gtt/min for 12 hours) with frequent monitoring of serum sodium levels because of suspected hyponatremic symptoms at the emergency room. Subsequent serum sodium concentrations thereafter were 113, 117, 119, and 121 mEq/L. After improvement in hyponatremic symptoms, his treatment was switched to isotonic saline infusion and furosemide (20 mg bid per os). The follow-up serum sodium level was 122 mEq/L and increased to 127 mEq/L at the time of a lung biopsy, which was performed through mediastinoscopy and revealed a neuroendocrine carcinoma. The patient underwent video-assisted thoracoscopic lobectomy of the left lower lobe with mediastinal lymph node dissection. The mass was revealed to be a 3×2.2 cm-sized LCNEC with visceral pleural invasion (Fig. 2). In addition, an enlarged interlobar lymph node was observed and removed. The final stage of LCNEC was T₂N₀M₀ (I_B). After surgical removal of the lung mass, his serum sodium concentrations were normalized (135 and 137 mEq/L) without any additional specific management. During the follow-up at an outpatient clinic, the patient received adjuvant chemotherapy with MAGE-A3 antigen-specific cancer immunotherapeutic, and hyponatremia did not recur.

DISCUSSION

SIADH is a common cause of hyponatremia in patients with malignancies.² Even though small cell lung cancer (SCLC) is responsible for more than 60% of tumor-associated SIADHs,³ SIADH may also occur in patients with non-SCLC as well as in patients with a variety of tumors.³ We herein report for the first time a case of SIADH in a patient with LCNEC of the lung, whose serum sodium levels were

completely normalized after surgical resection of the mass.

LCNEC is an uncommon tumor of the lung and belongs to the category of neuroendocrine tumors of the lung, along with typical carcinoid tumor, atypical carcinoid tumor, and SCLC.⁴ Since LCNEC has been regarded as a new type of lung cancer distinct from SCLC for only 20 years, the clinical features and prognosis thereof have not been extensively explored.⁵ Previous studies have demonstrated that most patients with LCNEC are male and have a heavy smoking history.⁵ In addition, no significant differences in the clinical symptoms and signs between patients with LCNEC and those with other lung cancers have been reported.⁵ In contrast to SCLC, no paraneoplastic phenomenon was observed at the time of diagnosis in 87 patients with LCNEC.⁶ On the other hand, Johnson, et al.⁷ reported a patient with LCNEC that developed hyponatremia and described a response of serum sodium levels during chest radiotherapy and chemotherapy. However, there has been no report of a case of SIADH in a patient with LCNEC of the lung, whose serum sodium levels were normalized after surgical resection of the mass. We surmise that this case may be the first report of SIADH in a patient with LCNEC, whose serum sodium levels were resolved after surgical resection of the mass.

Previous studies also demonstrated that SIADH may anticipate the diagnosis of malignancy several months in advance.⁸ In addition, SIADH is known to have a similar course to the underlying tumor.² Therefore, serial measurements of serum sodium levels in these patients during follow-up may be useful for monitoring the status of LCNEC.

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