Symptomatic Hyponatremia as the Initial Presentation of Small Cell Lung Carcinoma: A Case Report of Delayed Diagnosis

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Introduction

Lung cancer continues to add to the global health care burden, as it remains the leading cause of cancer related death in the United States. The CDC reports U.S. lung cancer incidence at 59.1 cases per 100,000. Compared to the national average, West Virginia has a higher reported incidence at 79.1 cases per 100,000. Small cell lung carcinoma (SCLC) is a subset of lung cancer accounting for 10-15% of total lung carcinomas diagnosed in the U.S. The relationship of SCLC and paraneoplastic syndromes, specifically the syndrome of inappropriate antidiuretic hormone (SIADH), has been well documented in the literature with its initial description in 1957. SIADH is a diagnosis of exclusion caused by an increased amount of ADH or an increased renal sensitivity to the hormone. The following criteria, known as the Bartter-Schwartz criteria, can be used to help differentiate SIADH from other causes of hyponatremia and includes: 4-7

- Low serum sodium (<135mEq/L)
- Low serum osmolarity (<270 mOsm/kg)
- Excessively concentrated urine (>100mOsm/L)
- Intact adrenal and thyroid function in a patient who is not taking diuretic therapy.

Mild hyponatremia can manifest as headache, nausea, and fatigue, whereas severe hyponatremia can present as altered mental status, loss of consciousness, seizure, coma or even death. 5-8

We present a case of SIADH diagnosed and first attributed to stroke; however, in retrospect was likely the initial presentation of an underlying SCLC.

Case Presentation

A 60-year-old Caucasian female presented to a single intensive care unit (ICU) in West Virginia on three separate occasions over a course of six weeks with symptomatic hyponatremia. Medical history was significant for hypertension, hyperlipidemia, atrial fibrillation, rheumatoid arthritis, uterine cancer and breast lobular carcinoma in situ. The patient was a current 2 pack-per-day smoker with a greater than 90 total pack-year smoking history. Her medications included aspirin, etanercept, methotrexate, folic acid, atorvastatin, metoprolol and esomeprazole/naproxen.

The patient received hypertonic saline (3% NS) for correction of hyponatremia and IV labetalol for elevated blood pressure. Her initial non-contrast head computerized tomography (CT) scan revealed no acute pathology and no cerebral edema; however, subsequent brain imaging over the course of a 16-day hospital stay revealed a right parietal-occipital lobe infarct with hemorrhagic transformation. The stroke was thought to result from her atrial fibrillation. Although she was on daily anti-platelet therapy, she was not on an anticoagulant. Electroencephalogram (EEG) performed on hospital admission showed no epileptiform activity. Repeat EEG on the 9th day of admission noted slight epileptiform discharges, which ultimately resolved on final EEG prior to discharge. The patient was placed on levetiracetam and warfarin for seizure prevention and anticoagulation, respectively, with an appointment to follow up with neurology and her primary care physician as an outpatient. The total hospital course involved 8 chest x-rays (CXR), all of which were within normal limits. Of note, during her hospital admission her methotrexate was discontinued per neurology recommendation.

Hospitalization #2:  
Length of stay: 4 days

One week later, the patient was admitted to the ICU with chief complaint of nausea and weakness. The patient reported history of chronic cough, non-productive and without hemoptysis, and shortness of breath, especially with exertion, but no recent weight loss. Her vital signs and physical exam were normal, but she was severely hyponatremic with...
serum sodium of 106 mEq/L. She received a thorough hyponatremia workup with differential diagnosis of SIADH versus hypovolemia. Laboratory work-up included:

- Serum Na+: 106 (Normal: 135-145 mEq/L)
- Serum Osmolality: 223 (Normal: 275-295 mOsm/kg)
- Urine Osmolality: 584 mOsm/L (Normal: 50-1400 mOsm/L)
- Urine Sodium: 21 mEq/L
- TSH and cosyntropin stimulation test: within normal limits (3.95 and 26, respectively)

The patient had an intact and appropriate thirst sensation. Her lab values indicated SIADH. The patient was treated with normal saline and discharged with serum sodium of 128 mEq/L. During this hospital stay of 4 days, the patient received 1 CXR, which showed no acute findings. Discharge instructions included changing levetiracetam to lamotrigine, fluid restriction of less than 1L per 24 hours, and to follow up with her neurologist, nephrologist and primary care physician as an outpatient.

Hospitalization #3:
Length of stay: 6 days

The patient was transferred to the ICU from an outlying facility 12 days after her most recent hospital discharge, again for nausea and weakness. Her serum sodium at presentation was 116 mEq/L. She was treated with hypertonic saline and tolvaptan (ADH receptor antagonist). After receiving the diagnosis of SIADH, she was subsequently transferred to the medicine floor for further workup of the SIADH etiology. A CT scan of her chest and abdomen was performed on hospital day 2, revealing left hilar lymphadenopathy, with the largest lymph node measuring 1.5 cm. A left suprahilar lung mass was also reported, measuring 3 cm X 3.4 cm X 4.2 cm (Images 1-2). Further oncologic workup included positron emission tomography (PET). Image 3 reveals the hypermetabolic activity of the mass on PET scan. The patient underwent endobronchial ultrasound with nodal and mass biopsy on hospital day 5. The pathology report confirmed a bronchial malignancy of small cell carcinoma subtype.

Discussion

The literature reports many causes of SIADH, the vast majority secondary to malignancy or medication. Other causes include primary pulmonary or central nervous system processes, HIV, hereditary causes, exogenous hormonal usage and idiopathic SIADH. Of note, the patient’s medication regimen on initial presentation included methotrexate and levetiracetam, both of which have been associated with SIADH, and were discontinued or changed to rule out a medication-induced cause of her hyponatremia on subsequent presentations.

Treatment of SIADH involves determination of the chronicity and hyponatremia severity. The safest and most commonly used management of SIADH is fluid restriction less than 800-1000mL per day so that urinary output exceeds oral fluid intake. When fluid restriction alone is insufficient, salt tablets in combination with loop diuretics, urea, demeclocycline, lithium, ADH receptor antagonists or a hypertonic saline bolus have been used. The most feared complication in hyponatremia correction is osmotic demyelination syndrome (ODS). ODS manifests with neurologic changes, the most severe of which is locked-in syndrome resulting from bilateral pontine demyelination. Patients are at greater risk of developing ODS when the Na+ levels are corrected >12 mEq in a 24-hour period and when the hyponatremia is more chronic in nature (>48 hours). Prevention of this often irreversible complication is with tightly controlled correction of Na+ levels, of about 8mEq/day.

When a patient presents with severe symptomatic hyponatremia, the therapy of choice is a hypertonic
saline (3%NS) bolus due to its rapid onset; however, this requires a consideration of risks versus benefit of treatment and close monitoring of Na+ levels and neurologic status.4,8 Our patient was treated with 3% NS on her first hospitalization due to severe hyponatremia manifesting as loss of consciousness. She was discharged from the second hospitalization with fluid restriction, and on her 3rd admission was treated with hypertonic saline and tolvaptan, a medication that antagonizes the action of ADH at the kidney.

The literature has reported that hyponatremia and SIADH is a poor prognostic indicator in SCLC.9,10 In a prospective study comparing the survival of patients with SCLC, Wang et al. concluded that patients with SIADH had decreased progression free survival and reduced overall survival when compared to controls with SCLC that did not have SIADH.10 Additionally, the Na+ levels of the majority of patients in this study normalized after a few rounds of chemotherapy,10 which is consistent with other current literature, emphasizing the importance of cancer diagnosis and oncologic workup as the hyponatremia may be treatable. This case serves as an example of a paraneoplastic syndrome presentation prior to receiving cancer diagnosis. This patient’s symptomatic hyponatremia was masked by her initial stroke presentation and her unremarkable chest x-rays. This case serves to remind clinicians that a patient presenting with hyponatremia warrants further investigation, including medication review along with urine studies, serum studies, thyroid function and adrenal function. Furthermore, patients with SIADH and an extensive smoking history may warrant further investigation for an underlying malignancy.

References