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| RESEARCH ARTICLE

A Seizure That Has Started in the Lungs: Unusual Presentation of Lung Cancer

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| ABSTRACT

It is hardly surprising that paraneoplastic syndrome could be the first sign of an underlying malignancy. Sometimes, a patient's condition is not apparent clinically but is revealed through laboratory findings, as they may appear clinically well while being biochemically unwell, such as in patients with the Syndrome of Inappropriate Anti-Diuretic Hormone Secretion (SIADH). This case report highlights SIADH and Small-Cell Lung Cancer (SCLC) as a classic clinical pairing in elderly smokers. It presents a 64-year-old Saudi male who was brought to the emergency department after experiencing new-onset generalized tonic-clonic seizures, despite having no prior history of epilepsy or any identifiable triggers for his symptoms. Laboratory workup revealed severe hyponatremia, with the patient being euvolemic on examination of his volume status, fulfilling the criteria for the textbook definition of SIADH. Management included cautious correction of his serum sodium levels using hypertonic saline boluses and fluid restriction. After stabilization, lung cancer was suspected based on chest CT imaging and later confirmed via lung biopsy. He was subsequently referred to a tertiary center for ongoing management of hyponatremia and definitive treatment of lung cancer.

| KEYWORDS

Lung Cancer, Paraneoplastic Syndrome, Hyponatremia, SIADH, Seizure

| ARTICLE INFORMATION

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1. Introduction

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is defined by the persistent unsuppressed release of excessive antidiuretic hormone (ADH), also known as vasopressin, despite the normal or increased extracellular fluid volume. Such excessive release of ADH results in hyponatremia and hypo-osmolality. In SIADH, there is impaired water excretion as kidneys retain free water, subsequently resulting in euvolemic dilutional hyponatremia [1]. Conditions that frequently lead to SIADH are variable and include central nervous system (CNS) disturbances—since any CNS abnormality can increase ADH release from the pituitary gland, such as stroke, hemorrhage, and infections; malignancies; pulmonary diseases (e.g., pneumonia and tuberculosis) and various medications Selective Serotonin Re-uptake inhibitors (SSRIs), carbamazepine, and chemotherapy agents [1]. From an oncological perspective, SIDAH is a well-known paraneoplastic syndrome, most frequently linked to and particularly prevalent in lung cancer cases. Epidemiological studies noted that approximately 70% of the cancer cases associated with SIADH arise from small-cell lung cancer (SCLC) [2]. Other reported malignancies to be associated with SIADH are

lymphomas, thymomas, mesotheliomas, and squamous cell carcinomas of the head and neck [2]. However, according to systematic reviews and meta-analysis studies of non–small-cell lung cancers (NSCLC), SIADH is a rare occurrence in non–small-cell lung cancers (NSCLC), affecting less than 1% of patients [2]. Therefore, SIDAH in the context of lung cancer is predominantly a feature of SCLC. Approximately 9-15% of patients with SCLC develop SIADH during their illness, with some series noting up to 10–45% over the disease course [3]. In comparison, NSCLC was noted to cause hyponatremia only in the advanced stages of the disease (e.g. brain metastases or postsurgical), and SIADH as an initial presentation in NSCLC is extremely rare [2][4]. Mechanistically, SIADH in the context of lung cancer is due to ectopic hormone production by tumor cells. Neuroendocrine cells in SCLC can aberrantly secrete vasopressin (ADH) independent of normal feedback, leading to unregulated water reabsorption in the renal collecting ducts [5]. This causes dilutional hyponatremia as water moves into cells, including brain cells. Some SCLC tumors also express atrial natriuretic peptide (ANP), but ADH remains the principal driver of the paraneoplastic SIADH syndrome [5]. The resulting hypotonic hyponatremia produces neurologic symptoms by causing cerebral edema. In mild or chronic hyponatremia, patients often have only subtle findings (nausea, gait disturbance), but as the serum sodium falls acutely, neurological toxicity worsens. In practice, severe hyponatremia (<120–125 mEq/L) often precipitates encephalopathy, seizures, and even coma [6][7]. For example, osmotic water shifts lead to brain swelling and increased intracranial pressure; studies show that neurological symptoms become apparent as sodium approaches ~120 mEq/L, and acute drops below 115 mEq/L frequently trigger generalized tonic-clonic seizures [6][7]. Despite these risks, seizure as the initial manifestation of paraneoplastic SIADH is unusual. One study noted that only about 5% of patients with severe hyponatremia (less than 125 mEq/L) experienced acute seizures [6]. Furthermore, the majority of SIADH cases are identified through progressive symptoms or during cancer-related therapy. Hence, whenever an adult presents with a first seizure attack, they would undergo a full neurological work-up, and only when hyponatremia is extremely severe; would physicians start considering SIDAH. Such delayed consideration can obscure the true cause of illness. Notably, paraneoplastic syndromes often precede the clinical diagnosis of cancer. Early recognition of SIADH is therefore critical because it may reveal an occult malignancy. Indeed, evidence suggests that identifying paraneoplastic SIADH can lead to earlier stage diagnosis; patients with SCLC who present with paraneoplastic syndromes are more likely to have limited-stage disease and improved outcomes [8]. A few reports highlight lung cancer discovered after seizure-inducing SIADH. For instance, Ize et al. described a patient with no respiratory complaints who presented with syncope and seizures from profound hyponatremia; evaluation revealed small-cell lung carcinoma as the cause [9]. Similarly, Kobayashi et al. reported SIADH as the heralding feature of an early-stage SCLC found during routine follow-up [10]. However, such cases remain rare in literature. They are often missed initially because seizures prompt evaluation for neurologic causes (e.g. epilepsy, brain lesions) rather than paraneoplastic syndromes, especially if respiratory symptoms are absent. In our case study, the seizures the patient encountered and experienced were ultimately attributed to lung-related SIADH– in effect, a "seizure that started in the lungs". Such a clinical presentation highlights and strongly suggests to clinicians that any unexplained acute hyponatremia and seizures in elderly smokers should raise concerns for a paraneoplastic etiology, necessitating immediate investigation, including chest imaging, to rule out and uncover any hidden tumor. In such settings, early detection of lung cancer is mandatory for effective, timely, and successful treatment, potentially leading to improved survival rates.

2. Case Presentation

2.1 Patient's history and Physical Examination

This case report outlines a 64-year-old Saudi male who has no history of epilepsy. He sought medical attention at the hospital after an episode of seizure, matching the description of generalized tonic-clonic seizures and accompanied by post-ictal symptoms displayed as fatigue and confusion. He began suffering from these episodes a week ago. As of late, these episodes have increased in frequency and duration. He was brought to the hospital by a family member after witnessing the event. No certain trigger was identified for these episodes, nor was a proceeding aura reported. Our patient gave no history of recent head trauma, febrile illness, alcohol withdrawal, or drug use. Stroke and Transient Ischemic Stroke (TIA) manifestations like dysarthria, hemiparesis, facial asymmetry, and other symptoms were notably absent. Thorough history taking was unremarkable for headache, visual disturbances, focal neurological deficits, cough, dyspnea, chest pain, or hemoptysis, yet it was positive for progressive fatigue, mild anorexia, and a 5-kg weight loss in the past three months. He has always been medically and surgically free, not taking any medications, but has been smoking one pack of cigarettes per day for the past 40 years. Alcohol use was expressly denied by the patient. Additionally, family history was noncontributory for any malignancies or epilepsy. Upon physical examination, he appeared alert, conscious, oriented, and afebrile with stable vital signs. Local examinations of the chest, cardiovascular system, the abdomen and nervous system were normal. Finally, no edema in his extremities nor signs of dehydration were noted by physicians.

2.2 Investigations

Extensive blood and urine tests had to be conducted, with results shown below (Table 1).

Test	Result	Normal Range
Sodium	112 mmol\L	135-145
Potassium	4.1 mmol\L	3.5-5.0
Bicarbonate	24 mmol\L	22-29
BUN	15 mg\dL	7-20
Creatinine	0.7 mg\dL	0.5-0.9
Fasting glucose	80 mg\dL	70-100
Calcium	9.2 mg\dL	8.5-10.2
TSH	0.6 mIU\L	0.4-4.0
Urine sodium	80 mmol\L	20-40
Urine osmolality	550 mOsm\kg	50-1200
Serum osmolality	260 mOsm\kg	275-295
Morning cortisol	Normal	-

Table 1: results of relevant investigations.

3. Management course

Since our patient came in a stable condition, able to maintain his airway with a Glasgow Coma Score (GCS) of 15\15, and his seizures were attributed to an electrolyte disturbance in the form of hyponatremia, no immediate antiseizure medication was required. The management for this case was set to focus on safe correction of hyponatremia. Because it was symptomatic, this hyponatremia was considered severe hyponatremia. Out of concern for Osmotic Demyelination Syndrome (ODS), the use of hypertonic saline for management of hyponatremia is often avoided, with symptomatic hyponatremia being an absolute exception. 3% hypertonic saline boluses (100mL over 10 minutes) were cautiously given to this patient, while monitoring serum sodium levels every 4-6 hours and aiming for a rise of 4-6 mmol\L in first 6 hours. Fluid intake was also restricted to less than 700mL\day. Serum sodium levels reached 119 mmol\L after 6 hours and 125 mmol\L after 24 hours. Once our patient became neurologically stable with a serum sodium that was maintained above the level of 125 mmol\L, boluses were stopped. Because blood and urine tests were consistent with SIADH, an immediate workup for causes of SIADH was conducted, including thyroid function tests, morning cortisol, and head and chest CT. As expected in an elderly smoker, SIADH is usually induced by paraneoplastic causes. This was really the case for this patient, as his chest CT demonstrated a right upper lobe mass, which was later confirmed by biopsy to be SCLC. This patient was transferred to a tertiary center for chronic correction and oncological management.

4. Discussion

Whenever there is a new-onset seizure in elderly patients, idiopathic epilepsy is rarely found to be the cause, and secondary causes, whether structural (e.g, trauma, hemorrhage, tumor) or metabolic (e.g, electrolyte abnormalities, hypoglycemia), must be investigated [9]. One commonly encountered reversible secondary cause is hyponatremia. Whether chronic or acute, it can cause significant cerebral edema leading to disruption of the brain's electrical activity and resulting in a lower seizure threshold as an outcome [5]. Hyponatremia is not a definitive diagnosis without classifying it into one of the three categories: hypovolemic, euvolemic, or hypervolemic. Many clinicians mislabel SIADH as 'fluid overload' when it is euvolemic in most cases [9]. Based on that, the absence of edema and signs of dehydration, in addition to the presence of hypotonic plasma osmolality despite inappropriately high urine osmolarity (>100 mOsm\kg), and high urinary sodium with normal thyroid, renal, and adrenal functions, all fulfill the criteria of SIADH, confirming it as a well-established diagnosis rather than a mere assumption [1]. It is wise to check TSH and cortisol in any patient presenting with SIADH, owing to the fact that hypothyroidism and adrenal insufficiency can mimic SIADH [1]. Notably, an important step in evaluating SIADH is to take a thorough medication history, as SIADH can be triggered by medications like carbamazepine, thiazides, and SSRIs [1][9]. It has been reported that around 10-15% of SCLC patients eventually develop SIADH, making malignancy stand out as a classic cause for SIADH in elderly smokers due to ectopic Anti-Diuretic Hormone (ADH) secretion without any negative feedback in response [3][4]. Though a history of heavy smoking hints at cancer, lung malignancy can still be present without any suggestive symptoms such as cough or hemoptysis [4]. While significant weight loss raises suspicion for malignancy, it is still extremely rare for symptomatic paraneoplastic SIADH to be the first sign of cancer [4]. In some malignancies, neurological symptoms can be attributed to possible brain metastases, warranting baseline contrast-enhanced MRI or CT of the brain for any new neurological symptoms, including seizures in patients with malignancy, and basically all newly diagnosed cases of SCLC as part of standard staging [4][9]. Importantly, when the neurological status of a patient with symptomatic hyponatremia is stable, safe correction of serum sodium levels is sufficient, deferring the need for antiseizure medications if the patient is not experiencing active seizures [10]. If seizures become recurrent,

short-term anti-seizure medications like benzodiazepines may be used [10]. As mentioned earlier, a gradual increase in serum sodium levels should be aimed for to avoid the devastating complication of ODS, with an ideal rate of 4-6 mmol\L in the first 6 hours and a maximum of 8-10mmol\L per 24 hours [9]. Though ODS have been reported more often as a complication of rapid sodium correction in chronic forms of SIADH, it can also occur in acute cases [9]. ODS typically presents with confusion and lethargy in the early phases, progressing to dysarthria, dysphagia, spastic quadriparesis and even irreversible locked-in syndrome, in which the patient is conscious but completely paralyzed, with control only over vertical eye movements [9]. If SIADH was chronic, oral demeclocycline might be necessary to achieve control, but it should be used with caution in the elderly due to its known nephrotoxicity, reserving oral tolvaptan for refractory hospitalized cases [10]. Fortunately, paraneoplastic SIADH often resolves after tumor treatment by chemoradiotherapy, making malignancy management the definitive treatment [10].

5. Conclusion

In an elderly patient, a first seizure is rarely idiopathic; hence, secondary causes must be thoroughly investigated. When hyponatremia is encountered, volume status is the key factor in identifying the root cause of hyponatremia, whether due to hypervolemia (as in cirrhosis and congestive heart failure), hypovolemia (secondary to gastrointestinal or renal losses), or euvolemia (as in cases of SIADH). For any severe euvolemic hyponatremia, the possibility of SIADH should not be underestimated, despite its rarity. Additionally, SIADH should be considered a red flag for malignancy in elderly patients, with small-cell lung cancer (SCLC) being the classic clinical association with SIADH. While patients with SIADH might appear clinically well, they are still biochemically unwell. Only laboratory tests can reveal the full depth of the problem in such cases. Finally, this case report highlights the crucial importance of thinking beyond common answers and encourages a broad and deep search in any case of seizure presenting to the emergency room. This underscores the need for a multidisciplinary approach, involving emergency physicians, internists, nephrologists, oncologists, and neurologists when necessary. Early recognition of SIADH can lead to the earlier diagnosis of malignancy in its limited stage.

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