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Unexpected Cause of Hyponatremia in Chronic Obstructive Pulmonary Disease ： Pituitary Adenoma

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Abstract

Hyponatremia in patients with chronic lung disease may be caused by a variety of disorders, but treatable, curable disorders may be overlooked. A 75-year-old man with chronic obstructive pulmonary disease (COPD) presented with an episode of syncope. He denied the use of diuretics or systemic steroids. He used oral bronchodilators for his lung disease. His blood pressure and volume status were normal. He had hyponatremia with a serum sodium level of 122 mmol/L. This was initially attributed to the very common syndrome of inappropriate secretion of antidiuretic hormone (SIADH). The hyponatremia persisted despite good control of the COPD. Measurement of hormones indicated hypopituitarism. Magnetic resonance imaging of the brain showed a pituitary macroadenoma in the sella. The tumor was removed by transsphenoidal surgery and the patient was treated with glucocorticoid and thyroid hormone replacement temporarily. His serum sodium normalized without further treatment. Nonfunctional pituitary adenoma with hypopituitarism should be kept in mind as a cause of hyponatremia in pulmonary diseases, especially in the elderly patients. (J Intern Med Taiwan 2007; 18: 360- 364)

Key Words ： Hyponatremia, Syndrome of inappropriate secretion of antidiuretic hormone, Chronic obstructive pulmonary disease, Pituitary adenoma

Introduction

Hyponatremia is the most common electrolyte disorder seen in hospitalized patients and may contribute substantially to morbidity and mortality. Patients with chronic obstructive pulmonary disease

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(COPD) are susceptible to hyponatremia for a number of reasons. Chronic hypoxia and hypercapnia secondary to the underlying pulmonary illness, heart failure or renal insufficiency, use of diuretics, SIADH, hypokalemia attributed to bronchodilators or steroids, malnutrition, and poor intake during acute exacerbations are common contributing factors for hyponatremia in such patients [1]. Activation of the renin-angiotensin-aldosterone system and inappropriately elevated plasma arginine vasopressin (AVP) in COPD may cause hyponatremia mimicking SIADH [2-4]. SIADH is associated with a number of pulmonary disorders, including pneumonia, tuberculosis, asthma, pneumothorax, lung cancer, bronchial adenoma, and positive-pressure ventilation, in addition to non-pulmonary causes such as diseases of the central nervous system, medications, severe stress condition, and ectopic AVP production [5-7]. The danger in managing a patient with COPD is simply attributing hyponatremia to SIADH without considering other causes. We report a case illustrating this point.

Case Report

A 75-year-old Chinese man had had mild COPD and hypertension for six years. He had a 30-to-40 pack-year smoking history. He reported dyspnea on exertion and a cough productive of yellow sputum for one month before admission. Medications within the previous six months included oral sustained release salbutamol 8mg/day and sustained release diltiazem 90 mg/day. He had not been treated with steroids, and he denied any recent weight gain or loss. He also drank 300 to 500 ml of water before sleep because of thirst, and his diet was generally bland. He was admitted because of an episode of syncope when he went to the toilet in the morning. He regained consciousness about one hour later when his family found him lying on the floor. He denied having a severe bout of coughing prior to the event, nor was it directly associated with either micturation or defecation. The patient was 170 centimeters tall and weighed 68 kilograms. His temperature was 36.7 ℃, pulse rate 90 per minute with a regular rhythm, respiratory rate 20 per minute, and blood pressure 130/80 mmHg without postural hypotension. His extracellular fluid volume appeared to be normal. There was paucity of axillary and pubic hair. On chest auscultation, left basal crackles were heard. The rest of the examination was unremarkable. In particular, there was no evidence of skull trauma, symptoms or signs of increases intracranial pressure, visual disturbance, neck rigidity, focal neurological deficits, Cushingoid changes, or abnormal skin pigmentation.

Table 1.Biochemical studies on admission

Plasma		Range	Urine	
Na^+(mmol/L)	122	135-147	Na^+(mmol/L)	55
K^+(mmol/L)	4.6	3.5-5.3	K^+(mmol/L)	30.9
Cl^-(mmol/L)	95	95-108	Cl^-(mmol/L)	75
Creatinine(mg/dl)	1.0	0.5-1.3	Creatinine(mg/dl)	68.9
Osmolality (mosm/kg)	260	285-295	Osmolality (mosm/kg)	337
Urea(mg/dl)	16	5-22	Volume(ml/day)	1,430
Uric acid(mg/dl)	3.6	2.5-7.5		

He had leukocytosis with a mild left shift (15900/ μl with 86% neutrophils). The only abnormalities on initial biochemical tests were a sodium of 122 mmol/L and a serum osmolarity of 260 mosm/kg (Table.1). Urine testing revealed a relatively high sodium excretion (55 mmol/L) and an inappropriately concentrated urine (337 mosm/kg). The electrocardiogram was normal. A chest x-ray film displayed increased bronchovascular markings in both lower lung fields. High resolution computed tomography of the lung demonstrated slight bronchial dilatation in the posterior basal segments of both lower lobes consistent with traction bronchiectasis as well as diffuse interlobular septal thickening and panlobular and centrilobar emphysema. He was thought to have an exacerbation of his COPD associated with a lung infection. Based on the serum and urine electrolyte data and the patient's euvolemic state, the hyponatrem-

Table 2.Results of hormonal tests

Test	Result	Range
Prolactin(ng/ml)	29.6	1-18
Human growth hormone (HGH)(ng/ml)	0.39	<5
Luteinizing hormone (LH)(mIU/ml)	<3	<25
Testosterone(ng/ml)	<0.2	1.81-7.72
Thyroid stimulating hormone (TSH)(μIU/ml)	1.36	0.50-5.15
Thyroxine,free (FT4)(ng/dl)	1.14	0.8-2.0
Adrenocorticotropic hormone (ACTH)(pg/ml)	41.2	9-52
Cortisol(8AM)(μg/dl)	8.4	5-20
Cortisol(5PM)(μg/dl)	4.59	2.5-10
Renin(supine)(pg/ml)	7.86	2.4-22
Aldosterone(supine)(pg/ml)	76.9	29.9-158.8

ia was attributed to SIADH secondary to his pulmonary disease. He was treated with broad-spectrum antibiotics which brought his pulmonary infection under control. However, after intravenous fluid administration of potassium chloride 20 meq added in normal saline 1,000 ml daily for two weeks, he remained hyponatremic with a serum sodium of 129 mmol/L. No explanation for his initial syncopal episode had been found, as there was no evidence of cardiovascular disease, a cerebral vascular accident, medication side effects, or orthostatic hypotension.

Further testing was undertaken and the patient was unexpectedly found to have partial anterior hypopituitarism, with an elevated prolactin level and low levels of human growth hormone, luteinizing hormone, and testosterone (Table.2). An MRI study of the brain with and without contrast enhancement revealed a pituitary tumor extending into the suprasellar area up to the inferior border of the optic chiasm (Fig.1). Bitemporal hemianopia developed three weeks later. The patient then underwent transsphenoidal resection of the pituitary tumor. We had started glucocorticoids and thyroid hormone replacement two days prior to surgery until one week after operation to cover the stress during and after tumor resection. Normal diet was initiated after surgery. The follow-up serum sodium levels on the first day and in the third week after operation had normalized to 139 mmol/L and 139 mmol/L respectively. The serum sodium level remained normal over the next three months of follow-up.

Fig.1.MRI of the sella with contrast enhancement on sagittal and coronal sections. The pituitary gland is enlarged, measuring from 14 to 16 mm and extends to the suprasellar area, contacting the inferior border of the optic chiasm. There was enhancement of the pituitary stalk enhances and is slightly displaced to the left. No involvement of the cavernous sinuses or abnormal enhancement in the hypothalamus is seen.

Discussion

The initial findings in our patient of COPD with secondary infection and impaired water excretion resulting in hypo-osmotic hyponatremia all seemed consistent with SIADH, a relatively common finding. SIADH is defined as excess secretion or action of AVP in a euvolemic patient without a commensurate reduction in fluid intake resulting in water retention and decreased plasma osmolarity and sodium[8,9]. Our patient met these criteria, with his history of nightly fluid intake and a bland diet further supporting the diagnosis. Free water administration combined with a low salt and solute intake further worsen hyponatremia when water excretion is impaired.

The degree of hyponatremia in patients with COPD generally correlates with the severity of the lung disease. It is particularly common in patients who are relatively hypercapnic and hypoxic and un-

der substantial physiologic stress, as may occur in severe COPD, serious secondary infection, or acute respiratory failure [2-4]. The hyponatremia should not be ignored, as it is a risk factor for a poor outcome of pneumonia in elderly patients [10,11]. But our patient's lung disease was not that severe, and his infection seemed to respond adequately to antibiotics. It was the persistence of the hyponatremia despite his improved pulmonary condition that prompted us to look for another cause of SIADH and led to the finding of partial anterior hypopituitarism secondary to a pituitary macroadenoma.

Hyponatremia alone is not uncommon in a patient with untreated hypopituitarism, where it is usually attributed to secondary hypothyroidism and/or hypocortisolism [12-14], but there are not many reports in the literature of SIADH directly caused by a pituitary tumor [15-20]. Proposed explanations of the SIADH associated with pituitary tumors include (a) chemical stimuli of the hypothalamus-neurohypophyseal-adrenal system [13,14] or (b) the tumor exerting local mechanical stress [16-19]. SIADH may develop in patients with pituitary tumors who have no evidence of pituitary dysfunction; in such cases removal of the tumor may resolve the SIADH [16-19].

Our patient's tumor was non-functioning, and he had only partial hypopituitarism. His serum sodium level remained normal after discontinuance of hormonal replacement over the next three months postsurgically. The thyroid and adrenal function had not yet been compromised. That makes it reasonable to hypothesize that his non-functioning pituitary macroadenoma exerted pressure on the stalk, inducing over-secretion of AVP, which resulted in SIADH. The MRI study showed evidence that the macroadenoma displaced the pituitary stalk slightly to the left (Fig.1). The postoperative return of his sodium to normal levels supports this hypothesis.

In summary, hyponatremia due to SIADH is not uncommon in patients with lung disease, but it should not be casually dismissed as a transient phenomenon secondary to the underlying disease. This is particularly important in elderly patients who may have a number of comorbidities and multiple medications that confuse the picture. At the very least, the history and physical examination should be carefully reviewed for any signs or symptoms of intracranial lesions. If the hyponatremia fails to resolve as the underlying lung disease improves, a search for other causes of SIADH should be undertaken to avoid missing potentially curable disorders.

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慢性阻塞性肺疾病的病人發生不可預期原因的低血鈉症：腦下垂體腺瘤

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摘　要

低血鈉症發生在慢性肺疾病病人的身上可以有很多不同造成的原因，但是一些可治療、可治癒的的疾病可能會被遺漏。我們報告一位七十五歲男性病人，他有慢性阻塞性肺疾病而且發生暈厥的表現。他除了使用支氣管擴張劑外，並無使用利尿劑及類固醇等藥物。他的血壓及體液狀態是正常的。最值得注意的是血鈉值是122 mmol/L 並且符合了抗利尿激素不適當分泌症候群（SIADH）的診斷標準。即使在良好的控制慢性阻塞性肺疾病之後，低血鈉仍然存在著。荷爾蒙的檢查顯示有腦下垂體功能性低下的情形，頭部核磁共振影像學檢查發現在腦下垂體處有一巨大腺瘤。在經蝶骨內視鏡手術移除腫瘤及住院中短期使用類固醇和甲狀腺素後，此後並不須其他治療，病人的血鈉仍然維持正常。在慢性肺疾病的病人身上發生低血鈉症的鑑別診斷，無功能性的腦下垂體腺瘤應該被列爲是其中之一，特別是在老年人族群。