Thymoma Associated With Syndrome of Inappropriate Antidiuretic Hormone Secretion and Myasthenia Gravis

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ABSTRACT: We describe the association of malignant thymoma with the syndrome of inappropriate antidiuretic hormone secretion and myasthenia gravis. Hyponatremia has not been reported associated with those tumors and our case should alert physicians about the potential for a life-threatening complication.

THE SYNDROME of inappropriate antidiuretic hormone (SIADH) secretion has been associated with three classes of disorders—carcinomas, pulmonary, and central nervous system abnormalities. The hyponatremia is due to abnormal water metabolism. There is high urine osmolality out of proportion to serum osmolality and high urine sodium concentrations. A diagnosis of SIADH may be made after excluding other reasons for decreased diluting capacity of the renal tubules, including renal, pituitary, adrenal, thyroid, cardiac, or hepatic diseases. The presence of non-osmotic stimuli for ADH release, such as hemodynamic derangements caused by hypotension, nausea, or drugs must be ruled out. The patients have had mental status changes, confusion, lethargy, seizures, psychosis, coma, or even death due to water intoxication of neuronal cells.[1,2]

We saw a patient with myasthenia gravis, thymoma, and hyponatremia. Although thymoma is listed as a disorder associated with SIADH,[2-4] a literature review did not reveal a study of this particular abnormality. We present the following unique clinical case.

CASE REPORT

Our patient was a 77-year-old white woman who had a 1-month history of right shoulder and neck pain. More recently, she had anterior chest pain and discovered a fixed lump between her right breast and sternum. She complained of increasing fatigue, difficulty walking, and problems with her speech. She denied fever, chills, sweats, weight loss, or shortness of breath. The patient had no significant medical history. She denied taking any medications or having drug allergies and had no history of tobacco or alcohol use.

On initial examination, the patient was noted to have a 3 cm x 4 cm fixed mass between her right breast and sternum. She had no lymphadenopathy, her lungs were clear, and there were no abdominal masses palpated. The patient exhibited proximal muscle weakness in all four extremities but had no muscle tenderness. She had no ptosis.

Laboratory tests were remarkable for sodium 125 mEq/L and lactate dehydrogenase 272 U/L. A chest radiograph revealed large lobulated retrosternal densities and ill-defined margins of the right 5th rib. A chest computed tomography (CT) scan revealed two mediastinal masses with distinct imaging characteristics—a lobulated low-density mass originating in the anterior mediastinum and extending to the anterior chest wall and a second lesion in the middle mediastinum that appeared vascular and enhanced similarly to thyroid tissue. The thyroid scan was normal. Bone scan showed increased uptake in the upper-third of the sternum. Mammogram and CT of the head were negative. An electromyogram revealed the presence of an inflammatory myopathy.

With the above findings and an elevated creatine phosphokinase, her condition was most consistent with polymyositis. The absence of muscle pain prompted a search for other disorders and a high anti-acetylcholine receptor antibody level was detected, which strongly suggested the presence of myasthenia gravis. A fine needle aspiration of the chest wall mass showed malignant cells. The patient was referred to our hospital.

While awaiting surgical biopsy, she became acutely confused. Laboratory values are shown in the Table. A diagnosis of SIADH was made and she improved with correction of the hyponatremia. Later, however, she developed muscle weakness and respiratory compromise despite treatment with steroids and pyridostigmine. The patient required mechanical ventilation and improved rapidly with plasmapheresis. A biopsy of the mediastinal mass revealed well-differentiated thymic carcinoma. The patient was treated with etoposide and cisplatin and had an excellent response. There was no recurrence of hyponatremia.

DISCUSSION

The systemic syndromes associated with thymomas include autoimmune or immune dis-

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TABLE. Laboratory Values

Serum Values	
Sodium	116 mEq/L
Chloride	82 mEq/L
Potassium	4.8 mEq/L
Carbon dioxide	26 mEq/L
Glucose	95 mg/dL
Blood urea nitrogen	13 mg/dL
Creatinine	0.5 mg/dL
Osmolality	239 mOsmol/kg
Calcium	9.3 mg/dL
Uric acid	1.3 mg/dL
Total protein	6.8 g/dL
Albumin	4.2 g/dL
Creatine phosphokinase	1,149 U/L
Lactate dehydrogenase	480 U/L
Cortisol	19.8 µg/dL
Thyroid-stimulating hormone	3.99 µIU/mL
Renin	1.6 ng/mL/hr
Creatinine clearance	99 mL/min
Serum acetylcholine receptor antibody	28.9 nmol/L (normal less than 0.02 nmol/L)
Antinuclear antibody	negative
Urine Values	
Sodium	88 mEq/L
Chloride	78 mEq/L
Potassium	48 mEq/L
Osmolality	434 mOsmol/kg

orders, endocrine disorders, non-thymic cancer, severe infections, and other diseases. These conditions often lead to the discovery of the tumor. Generally, 70% of thymoma patients have immunologic disorders, 10% have malignancy, 5% have an endocrine disorder, and the remaining have severe infections or unrelated conditions. Between 30% to 50% of thymoma patients have myasthenia gravis. Some patients may exhibit more than one disorder,[5] as in our case.

In this patient, thymoma was associated with myasthenia gravis, polymyositis, and SIADH. While there are published reports of thymoma and polymyositis, we could find no other paper in the available literature describing the phenomena of SIADH and thymoma. The hyponatremia might have been due to the presence of lung pathology, a typical stimulus for the development of SIADH, or it could be attributed to the patient's thymoma. We favor the latter, based on the effect of therapy. Our patient had no further problems with hyponatremia once treatment was instituted and the tumor rapidly responded. No other form of long-term therapy was given and this suggests a causal relationship rather than chance/temporal association.

Classically, SIADH has been associated with bronchogenic carcinoma with 2% incidence. The mechanism involves ectopic production of an ADH-like substance by the tumor.[6-10] The pathophysiology of SIADH development in thymoma remains to be elucidated. Nevertheless, it adds to the interesting associations characteristic of this tumor. We hope to alert physicians to look for early clues for a serious complication in patients with thymoma.

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