



## Squamous Cell Carcinoma of the Larynx with Syndrome of Inappropriate Secretion of Antidiuretic Hormone

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### Authors' contributions

*This work was carried out in collaboration between all authors. Author MVM wrote the draft of the manuscript. Author CDL managed the literature searches. Author JCF provided the case and managed the literature searches. Author JADP contributed to write the draft of the manuscript and supervised the work. All authors read and approved the final manuscript.*

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Case Study

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### ABSTRACT

**Background:** Paraneoplastic syndromes result from the secretion of hormones by a tumor giving rise to different syndromes. Lung carcinomas are the most common tumors causing paraneoplastic syndromes. The most common is the syndrome of inappropriate secretion of arginine vasopressin (SIADH).

**Objective:** To describe the case of a patient with larynx cancer and secondary SIADH and review of the literature.

**Case Report:** We present the case of an 80-year-old man with dry cough, dysphonia and severe hyponatremia. Physical examination was unremarkable. After admission he developed acute stridor and a tracheostomy was performed. Serum and urine analysis confirmed the presence of SIADH in the absence of renal, adrenal or thyroid dysfunction. No SIADH producing drugs were reported. An

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ORL examination revealed the presence of a thickened area just below the right vocal cord. Hystopathological examination was suggestive of squamous cell carcinoma. After total laryngotomy, the final hystopathological exam reported the presence of a well differentiated squamous cell carcinoma. Hyponatremia was corrected with restriction of water intake to a maximum of 500 cc daily. Concomitant radiotherapy was administered.

**Conclusion:** Ectopic or inappropriate hormone secretion is uncommon in patients with the head and neck cancer. However, this condition should be included in the differential diagnosis of SIADH.

*Keywords: Larynx cancer; SIADH; paraneoplastic syndrome; squamous cell carcinoma.*

## 1. INTRODUCTION

Paraneoplastic syndromes can be defined as systemic and non-metastatic manifestations associated with a wide variety of malignant neoplasms. Usually these paraneoplastic syndromes affect a minority of cancer patients. They result from the secretion of hormones by a tumor giving rise to different syndromes that can involve the skin, the endocrine system, or can be hematologic, neurologic, or osteoarticular. Lung carcinomas, especially oat cell carcinoma and squamous cell carcinoma, are the most common tumors causing paraneoplastic syndromes [1]. Among all of these paraneoplastic syndromes, the most frequent is the syndrome of inappropriate secretion of arginine vasopressin, also known as Schwartz-Bartter syndrome or as syndrome of inappropriate secretion of antidiuretic hormone (SIADH). It was first described by Schwartz et al. [2] in patients with bronchogenic cancer. The most frequent oncological cause of SIADH is small cell lung cancer but it has been associated with many different types of tumors like pancreatic carcinoma, duodenal carcinoma, prostatic carcinoma, bladder carcinoma, mesothelioma, lymphomas, Hodgkin's disease, acute myelogenous leukemia, thymoma, small cell carcinoma of the esophagus and adrenocortical carcinoma. Characteristically, patients with SIADH present hyponatremia without edema. There is sodium dilution in a larger extracellular fluid volume and higher than normal sodium urinary excretion. This is caused by a decreased reabsorption in the proximal renal tubular tract because of the increased extracellular fluid volume.

Ectopic or inappropriate hormone secretion causing clinically manifest syndromes is uncommon in patients with head and neck cancer [3]. We described the case of a patient with larynx cancer and secondary SIADH and review the literature.

## 2. CASE REPORT

An 80-year-old man was admitted to hospital because of intense dyspnea in the presence of dry cough. He had been attended an otorhinolaryngologist consultation in the last month because of dysphonia showing on laryngeal examination the presence of bilateral palsies of vocal cords. He has a history of type 2 diabetes mellitus, hypertension and cerebrovascular ischemic disease 10 years ago without neurological impairment. He had smoked 25 packages/year until 10 years ago and reported no alcohol consumption. Physical examination revealed normal head and neck examination as well as chest, abdomen and neurological examination. He has no edema or ascites. Serum biochemistry showed severe hyponatremia (108 mEq/L) with other serum parameters in normal ranges. After admission the patient developed acute stridor and a tracheostomy was performed. In the following days several analytic tests were performed: serum osmolality 226 mOsm/L, urine osmolality 385 mOsm/L and urinary sodium concentration 83 mEq/L. Thyroid and adrenal function tests were normal. An ORL examination revealed the presence of a thickened area just below the right vocal cord. Hystopathological examination of biopsy specimens were non diagnostic because of intense bleeding. Under surgical examination new biopsy specimens were suggestive of squamous cell carcinoma so total laryngotomy was performed. The final hystopathological exam reported the presence of a well differentiated squamous cell carcinoma that infiltrates the thyroid cartilage. Hyponatremia was corrected with restriction of water intake to a maximum of 500 cc daily. Concomitant radiotherapy was administered. After 2 years of follow-up the patient developed metastatic disease and died.

## 3. DISCUSSION

Association of SIADH and head and neck cancer can be more common than thought. It has been

reported a 3% incidence of SIADH among patients with head and neck cancers [3]. The most common site of occurrence is the oral cavity in up to 40% of all cases. Larynx is involved in up to 18% and the nasopharyngeal area in 12% cases. Other less frequent areas involved are the hypopharynx, the nasal cavity, the maxillary sinus, parapharyngeal space, salivary glands and oropharynx [4]. The most common histologic tumor type is the squamous cell carcinoma [5].

SIADH may precede the presentation of the cancer by a few weeks or months, like in our patient or be observed after induction chemotherapy (especially when cisplatin or 5-fluorouracil are administered) for advanced disease or after neck dissection [6-8]. Manifestations of SIADH depend on its grade. In this sense, in mild SIADH (serum sodium concentration 130-135 mEq/L, or gradual development over several weeks) symptoms may be absent or limited to nausea, anorexia and vomiting. In cases of severe or acute hyponatremia, the most important symptoms are body weight increase, weakness, lethargy, confusion, convulsions and coma [9].

Diagnosis of SIADH should be considered in a patient with hyponatremia, (less than 135 mEq/L), urine osmolality greater than 100 mOsm/Kg and serum osmolality less than 275 mOsm/Kg. Urinary sodium concentration is usually greater than 40 mEq/L. The absence of edema, orthostatic hypotension, dehydration and the normality of thyroid and adrenal function test also points to the diagnosis of SIADH [10]. The clinician should exclude other causes of hyponatremia like dilution, edema states, hypertensive states, primary polydipsia, pseudohyponatremia, sick-cell syndrome, essential hyponatremia or side effect of several therapeutic drugs [11].

Traditionally, treatment includes limiting fluid intake, administration of hypertonic saline solution, diuretics such as furosemide, demeclocycline and, at present, the use of a competitive vasopressin receptor 2 antagonist such as conivaptan or tolvaptan [12,13].

#### 4. CONCLUSION

Overall, SIADH is the most common paraneoplastic syndrome. Lung carcinomas are the most common tumors causing these syndromes. Although SIADH is uncommon in

patients with head and neck cancer, it can be more common than thought. SIADH may precede head and neck diagnosis or occur after induction chemotherapy or neck dissection. In a patient with hyponatremia, the presence of SIADH should be investigated. If a diagnosis of SIADH is established, the presence of an associated tumor, especially lung carcinoma, must be investigated. Head and neck cancer should be considered in the differential diagnosis.

#### CONSENT

It is not applicable.

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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