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Review Article

Neuroendocrine Tumor of the Larynx

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Abstract

Neuroendocrine tumors are rare and can affect many organs, including the gastrointestinal tract and bronchi. The involvement of the larynx is exceptional, although neuroendocrine tumors are the second histological type of laryngeal malignancy after squamous cell carcinoma. They constitute a group of heterogeneous tumors, 4 in number, among the neuroendocrine tumors of the larynx, the carcinoma tumor neuroendocrine poorly differentiated is the most common. The diagnosis is purely histological, and the treatment is surgical. The prognosis is relatively good.

Keywords: Neuroendocrine tumor – Larynx – Immunohistochemistry – Surgery.

INTRODUCTION

Neuroendocrine tumors are rare and can affect many organs, including the gastrointestinal tract and bronchi. The involvement of the larynx is exceptional, although neuroendocrine tumors are the second histological type of laryngeal malignancy after squamous cell carcinoma. They constitute a group of heterogeneous tumors, 4 in number, whose clinical presentation, evolution and prognosis are not tumor type. Through a case of a slightly different neuroendocrine tumor of the larynx and a review of the literature, the authors are reminded of the main characteristics of this tumor.

OBSERVATION

This is a 69-year-old patient who is chronically ill with 30 packets a year stopped; without significant pathological antecedent. He consulted in ENT for anterior cervical swelling (Figure-1). The interrogation made it possible to note the existence of a dysphonia since about 4 months, of progressive worsening, as well as a dyspnea of the inspiratory type, first with the efforts, which evolved to become permanent requiring a tracheotomy safety. In addition, there was no dysphagia, no notion of impairment of the general state, carcinoid syndrome or other paraneoplastic syndromes. Endoscopic examination under sedation revealed a voluminous glotto-supra-glottic submucosal tumor, lateralized on the right, and obstructing almost all of the glottic space. The piriform sinuses and the subglottis were free. Biopsies were performed at the same time. The remainder of the examination revealed no palpable cervical lymphadenopathy or other abnormalities. Cervical computed tomography (CT) showed a tumor process of the right hemilarynx, slightly enhancing after iodinated contrast agent iv injection, resulting in lysis of the thyroid cartilage, with extension to the cervical soft tissues without invasion of the hypopharynx (Figure-2).

There were no lymphadenopathies visible on CT. The anatomopathological study of the biopsy showed that the tumor proliferation was made of medium-sized cells with a scanty and poorly defined cytoplasm, and nuclei increased in volume, irregular, hyperchromatic with rare nucleoli. Immunolabeling with the antichromogranin antibody showed focal positivity, and the anti-CD56 antibody was weakly positive. This aspect was in favor of a little differentiated carcinoma. The extension assessment found no secondary localization or other endocrine neoplasia, since the neuroendocrine tumor of the larynx can enter into multiple endocrine neoplasia type II. The patient underwent total laryngectomy with double lymph node dissection of functional type, involving groups II, III and IV (Figure-3). The postoperative course was simple. The anatomopathological result on the excision specimen was in agreement with that of the biopsy, namely a poorly differentiated carcinoma of the neuroendocrine type, whose exeresis limits were healthy. The anatomopathological study of the cleaning room did not reveal lymph node metastases. The patient benefited from complementary radiotherapy. The evolution after one year is favorable, without signs of local or general recurrence.

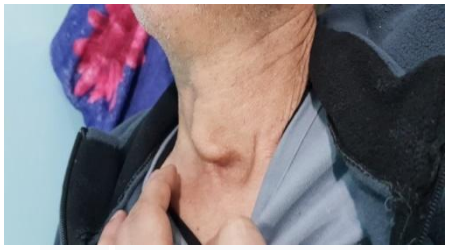

Fig-1: Anterior cervical swelling

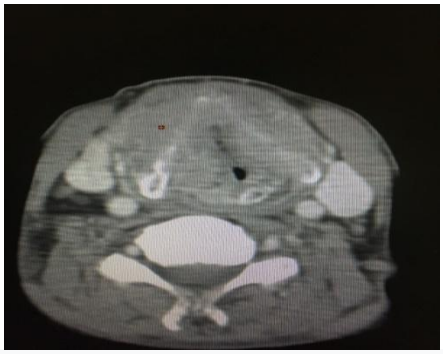

Fig-2: Computed tomography in axial section showing the voluminous laryngeal tumor process filling the glottic space and resulting in the lysis of the thyroid cartilage

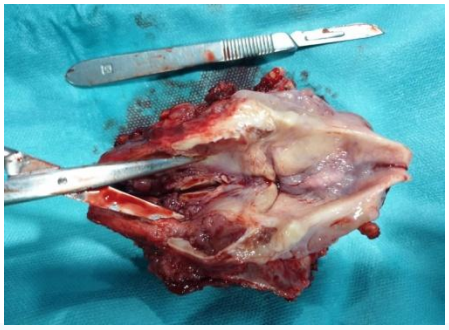

Fig-3: Macroscopic view of the laryngectomy

DISCUSSION

Neuroendocrine tumors of the larynx were first described in 1955 by Blanchard and Saunders [1], but the first case of neuroendocrine tumor with little differentiation was only reported in 1969 by NC Goldman *et al*., [1]. They represent 0.6% of all malignant tumors of the larynx, and are second in frequency after squamous cell carcinoma. The World Health Organization (WHO) classified them into 4 categories in 1991, according to their degree of differentiation:

- The typical carcinoid tumor, or well-differentiated neuroendocrine carcinoma, of epithelial origin, seen in 3% of cases;
- The atypical carcinoid tumor, or moderately differentiated neuroendocrine carcinoma, of epithelial origin, which represents 54% of cases, and which was the case of our patient;
- The small cell neuroendocrine tumor, or undifferentiated neuroendocrine carcinoma, of epithelial origin, which occurs in 34% of cases, and which was the case of our patient;

Paraganglioma, which represents 9% of cases, and is of neuronal origin [2]. A. Ferlito *et al*., published in 2006 a general review on neuroendocrine tumors of the larynx, listing more than 450 publications on this subject [2]. These various articles reveal several characteristic elements of the neuroendocrine tumors of the larynx, which we will try to summarize in this work. At the epidemiological level, they mainly affect men (sex ratio of 3/1), mean age between 60 and 70 years, except in the case of paraganglioma, which is more common in younger women (50 years). As with epidermal carcinoma, tobacco is the main risk factor [2, 3] Clinically, neuroendocrine tumors appear, like all other laryngeal tumors, with permanent dysphonia of progressive worsening, sometimes with neck pain. Dysphagia and dyspnea and the presence of a cervical mass are observed at more advanced stages [3, 4]. Paraneoplastic syndromes are rare in neuroendocrine tumors of the larynx; only a few cases of carcinoid syndromes have been described, most often associated with the presence of liver metastases. Other paraneoplastic syndromes, such as Schwartz-Bartter syndrome, Lambert-Eaton syndrome, or Cushing's syndrome, have been reported in typical carcinoid tumors [2, 5]. The endoscopic assessment makes it possible to objectify the tumor, which is generally submucosal, sometimes ulcerated, especially in cases of poorly differentiated tumors. It usually sits at the supra-glottal and / or glottal level. However, there is no evidence to distinguish it from epidermoid carcinomas [6]. The biopsy with histological study and especially immunohistochemical examination will allow to make the diagnosis. Thus, on the anatomopathological level, one finds a cellular pleomorphism important, with net cell atypies, prominent nucleoli, numerous mitoses and tumor necrosis. However, this aspect is not characteristic, and several differential diagnoses may arise, including undifferentiated carcinoma, adenocarcinoma or malignant melanoma. Immunohistochemistry is therefore essential for the diagnosis and classification of neuroendocrine tumors of the larynx. Several markers are used; the atypical carcinoid tumor responds positively to chromogranin A, synaptophospin, calcitonin, serotonin, somatostatin, CD56, CD57 and neurospecific enolase [7, 8]. The locoregional extension assessment should include cervical CT, looking for a contraindication to partial laryngectomy, and especially cervical lymphadenopathy. Lymph node metastases are present in 43% of cases [3]. The search for distant metastases is essential and is based on a chest x-ray, sometimes even a thoracic CT and abdominal ultrasound. Indeed, the frequency of metastases is estimated at more than 60% of cases. They sit preferentially in the skin or subcutaneous tissues, lungs, liver, bones, brain and peritoneum [2, 4]. They are often the cause of death of the patient, more than locoregional extension. A

biological assessment will also be performed, in search of multiple endocrine neoplasia; it is based on the determination of calcitonin and parathyroid hormone [2, 5]. The treatment of the neuroendocrine tumor of the larynx is surgical. The gesture will depend on the locoregional extension of the tumor; supra-glottal laryngectomy is often indicated, but total laryngectomy is required in case of extensive tumor, as for our patient. A bilateral ganglionic dissection of functional type carrying groups II to IV is also performed, even for N0 cases, because of the frequency of lymph node metastases [3].

Finally, undifferentiated neuroendocrine carcinoma is a relatively aggressive tumor: the 5-year survival rate is 46% [4].

CONCLUSION

Among the neuroendocrine tumors of the larynx, the carcinoma tumor neuroendocrine poorly differentiated is the most common. The diagnosis is purely histological, and the treatment is surgical. The prognosis is relatively good, compared with other types of neuroendocrine tumors.

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