Neuroendocrine carcinoma of the epiglottis. Case report

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Case Report

ONCOLOGIC SURGERY

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Abstract: Neuroendocrine carcinoma is a rare disease, represent less than 1% of the tumors of the larynx, moderately differentiated neuroendocrine carcinomas are the most common type of laryngeal neuroendocrine carcinoma and due to their relatively higher frequency, the majority of cases occur in male patients with a mean patient age of 61 years (range, 36-83 years). Neuroendocrine carcinomas are classified according to their cellular differentiation into well-differentiated neuroendocrine carcinoma, moderately differentiated neuroendocrine carcinoma, and poorly differentiated neuroendocrine carcinoma. The moderately differentiated neuroendocrine carcinoma tumors present as supraglottic masses in the arytenoids, epiglottis, or aryepiglottic folds, commonly causing hoarseness or dysphagia, It is relatively aggressive and has a greater propensity for regional and distant failure, leading to a worse prognosis. The mainstay of treatment for moderately differentiated carcinoma of the larynx is surgical excision. We present a 41-year-old caucasian female, with 1 year of evolution with a sensation of pharyngeal globus, who presents moderately differentiated neuroendocrine carcinoma, and was treated with conservative management, with good evolution, Treatment is based on resection, polychemotherapy, and concomitant radiation therapy. The prognosis is dire with a 5-year survival rate of 5%.

Keywords: Epiglottis carcinoma, neuroendocrine tumor, neuroendocrine carcinoma.

Introduction

The larynx is the most common site for head and neck cancer, however, laryngeal cancer is rare. [1] Laryngeal cancer represents 2% to 5% of new cancer in the world. [2] Neuroendocrine carcinoma of the larynx represents less than 1% of laryngeal tumors. [3] The máximum incidence is seen in men ranging between 50-83 years of age and heavy smokers, the male-to-female ratio of 45:10. It accounted for approximately 1% of all new cases in men and 0.3% of all new cases in women. [4, 5]

Epithelial cancer with neuroendocrine differentiation can occur in any organ of the body. Laryngeal tumors with neuroendocrine morphology are uncommon, heterogeneous groups, with specific morphological and histoimmunochemical characteristics. [6]

Laryngeal neuroendocrine neoplasms are divided into 2 broad categories base on their tissue of origin: epithelial and neural. In 1991 the WHO classifies neuroendocrine tumors of the larynx under 5 categories, 1) typical carcinoid (well-differentiated neuroendocrine carcinoma, grade I), 2) atypical carcinoid (moderately differentiated neuroendocrine carcinoma, grade II), 3) small cell carcinoma (poorly differentiated neuroendocrine carcinoma, grade III), 4) large cell carcinoma (grade II) and 5) combined cell carcinoma. [1, 4] The recent 2017 WHO Classification of Head and Neck Tumors has endorsed these changes and lists large cell neuroendocrine carcinoma and small cell neuroendocrine carcinoma under the rubric of poorly differentiated neuroendocrine carcinoma, which aims to combine histology and clinical behavior in one terminology: well-differentiated neuroendocrine carcinoma, moderately differentiated neuroendocrine carcinoma, and poorly differentiated neuroendocrine carcinoma. [7]

The moderately differentiated neuroendocrine carcinomas are the most common type of laryngeal neuroendocrine carcinoma and, due to their relatively higher frequency, their clinophatologic features are better understood. [7]

The tumors present as supraglottic masses in the arytenoids, epiglottis, or aryepiglottic folds, commonly causing hoarseness or dysphagia, Similar to well-differentiated types, they may appear as polypoid or submucosal in association with surface ulceration. Their size varies from a few millimeters up to 4 cm in diameter; upon sectioning, they exhibit a tan-white

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surface. [1, 5, 7]

It is relatively aggressive and has a greater propensity for regional and distant failure, leading to a worse prognosis.[1]

Treatment is based on resection, polychemotherapy, and concomitant radiation therapy. The prognosis is dire with a 5-year survival rate of 5%. [8]

Case report

41-year-old caucasian female, with 1 year of evolution with sensation of pharyngeal globus, 1 month of evolution with progressive dysphagia, odynophagia, cough, difficulty sleeping and breathing in the right decubitus position, on physical examination multiple cervical nodes are palpated in bilateral levels IA, IB, IIA, IIIB, III and IV, a rhino-fibrolaryngoscopy is performed where a rounded lesion is observed, with a polypoid appearance, smooth and mobile, in the vallecula of the epiglottis measuring 2.5 cm x 2.3 cm x 1.5 cm **(Figure 1)**. by which an excisional biopsy is performed, obtaining a hard, smooth tumor with a polypoid appearance, semi-pediculate, from the free edge of the epiglottis on the right side.

Microscopic analysis of the sample sent to pathology, who reported moderately differentiated malignant neoplasia. Immunohistochemical study was performed using monoclonal antibodies, finding CD-56 positive, Ki67 Positive in 15%, Protein s-100 negative, CD-34 negative, Calponin Negative, p63 Negative, Cytokeratin Coctail Negative, compatible with moderately differentiated neuroendocrine carcinoma. **(Figure 2)**

A multi-slice PET / CT was performed with administration of 68Ga-DOTANOC with an irregular thickening at the level of the epiglottis, left parasagittal of the middle epiglottic glossy fold, and of epiglottic cartilage with an asymmetry of the volume of the left epiglottic vallecula, associated with the presence of cervical ganglia in levels bilateral IA, IB, IIA, IIIB, III and IV that may correspond to an inflammatory process, with no increase in radiopharmaceutical uptake **(Figure 3)** without ruling out tumor activity.

The patient is treated with 70 Gy neck radiotherapy in 35 sessions with laryngeal cage technique, subsequently, multislice PET / CT is performed with administration of 68Ga-DOTANOC with axial cuts of the skull to the proximal third of the thighs, with no evidence of radiopharmaceutical uptake, nor on the expression of somatostatin receptors. Currently asymptomatic patient, under surveillance, without the presence of disease.

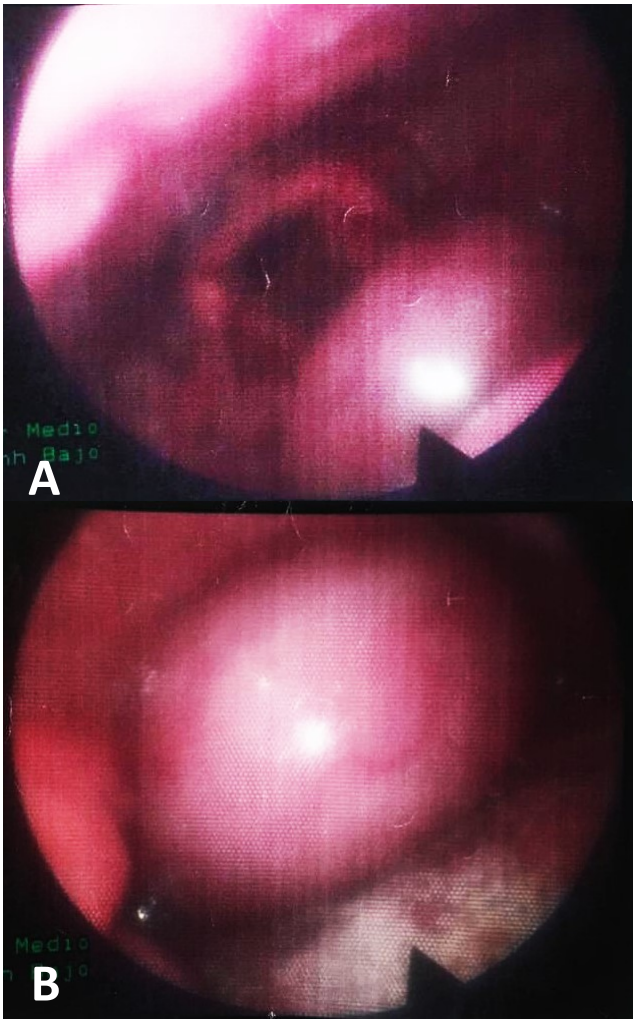

Figure 1. A and **B.** Rhino-fibrolaryngoscopy showing lesion polypoid appearance, smooth and mobile, in the vallecula of the epiglottis measuring 2.5 cm x 2.3 cm x 1.5 cm

Discussion

Head and neck cancer is a very heterogeneous disease that includes a large number of tumors with different clinical and etiological characteristics. The vast majority of them are squamous cell carcinomas, which constitute 95% of malignant tumors of the larynx. [9]

Neuroendocrine tumors of the larynx represent less than 1% of the tumors of the larynx, as in our clinical case. [10]

Moderately differentiated neuroendocrine carcinomas are the most common type of laryngeal neuroendocrine carcinoma and due to their relatively higher frequency, their clinicopathologic features are better understood. The majority of cases occur in male patients with a mean patient age of 61 years (range, 36-83 years) and a history of heavy tobacco smoking. Historically, four cases associated with carcinoid syndrome have been reported; however, in retrospect at least one of these cases is currently better classified as a large cell neuroendocrine carcinoma. The tumors present as supraglottic masses in the arytenoids,

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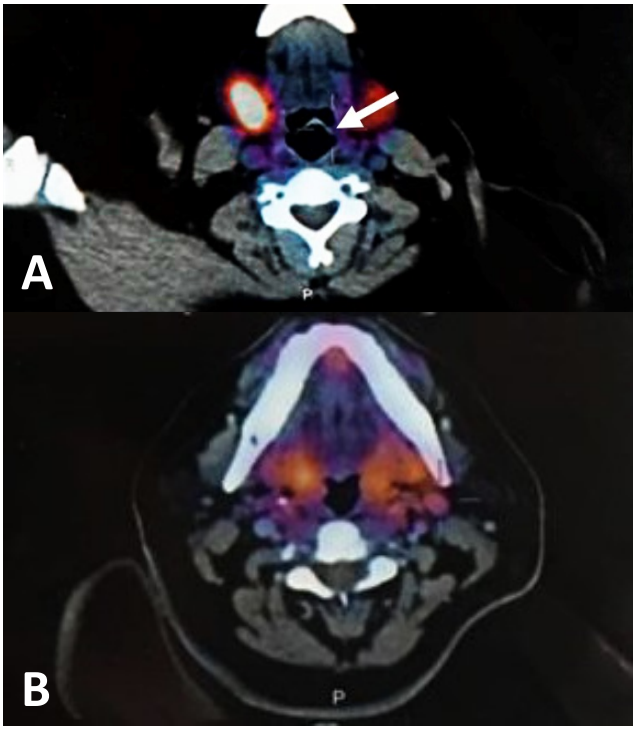

Figure 2. A. PET / CT with administration of 68Ga-DOTANOC a) with irregular thickening at the level of the epiglotis, left parasagittal of the middle epiglottic glosso fold and of epiglottic cartilage with asymmetry of the volume of the left epiglottic vallecula (White Narrow). **B.** Presence of cervical ganglia in levels Bilateral IA, IB, IIA, IIIB, III and IV

epiglottis, or aryepiglottic folds, commonly causing hoarseness or dysphagia. Similar to well-differentiated types, they may appear as polypoid or submucosal in association with surface ulceration. [7]

Their size varies from a few millimeters up to 4 cm in diameter; upon sectioning, they exhibit a tan-white Surface

The identification of more than two mitoses per 2 mm2 or 10 hpfs and/or necrosis are the main criteria separating moderately from well-differentiated laryngeal neuroendocrine carcinoma. [7]

The immunohistochemical pattern for neuroendocrine carcinoma includes positivity for Chromogranin, ACE, and CD56; the main differential diagnoses are paraganglioma, adenocarcinoma, and medullary thyroid cancer metastasis. [4]

The clinical and pathological features of carcinoma neuroendocrine are characteristic of the organ of origin, however, these tumors can share other attributes irrespective of their anatomical site. Functioning tumors, particularly carcinoid neuroendocrine tumors, can present with symptoms caused by hormone secretion; for example, patients may present with carcinoid syndrome, which is characterized by flushing, diarrhea and abdominal pain. [11, 12]

The mainstay of treatment for moderately differentiated neuroendocrine carcinoma de larynx is surgical excision. [13, 14]

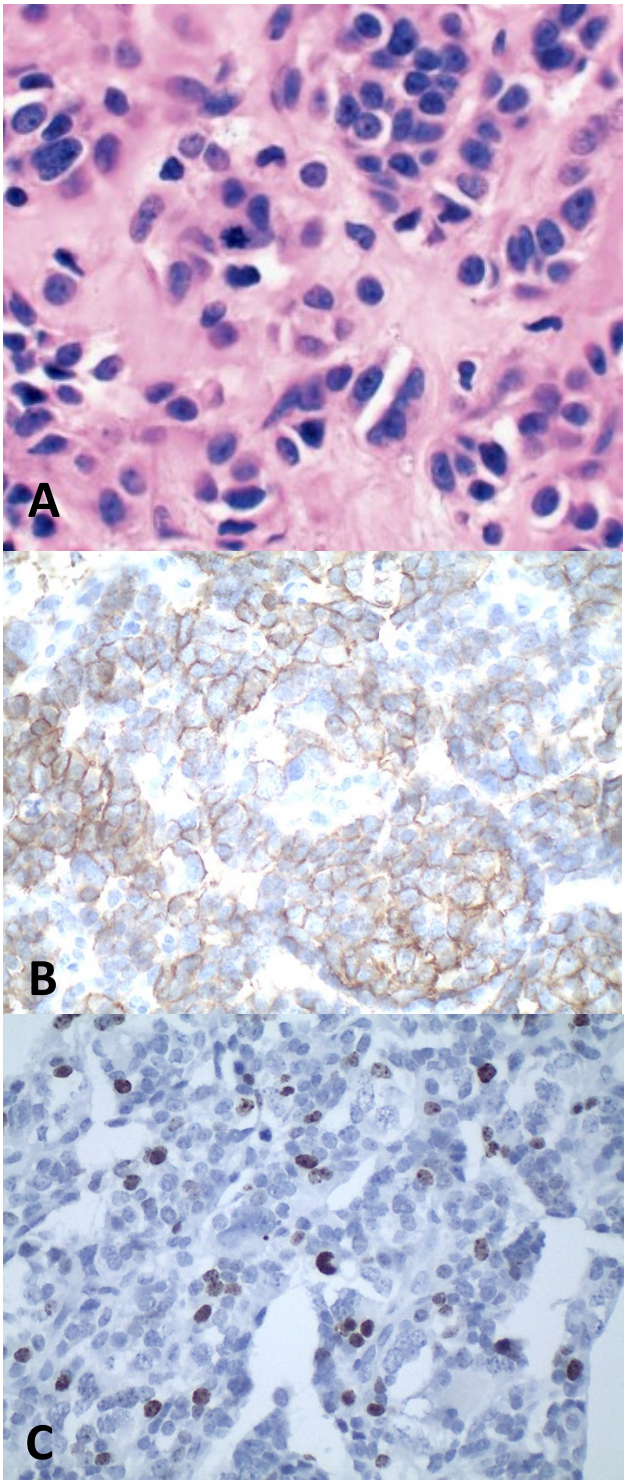

Figure 3. A. Moderately differentiated neuroendocrine carcinoma. High power field showing cells with mild pleomorphism and one mitosis (x600). **B.** Immunoreactivity to CD-56. **C.** Increased proliferation index 15% Ki67.

The chemotherapy employed preoperative, posoperative, or as a primary modality were ineffective in the management of this neoplasm. [15]

The clinical course of moderately differentiated neuroendocrine carcinoma is not indolent, as was believed in the past, Soga et al observed that 33.3% of 42 patients also developed metastases. [7]

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The majority of patients with moderately differentiated neuroendocrine carcinomas of the larynx present at early stage disease, while approximately 30% present with early distant metastases and advanced stage. Metastatic disease to the lung, bone, and liver has been reported in 38% to 44% of cases, while skin and subcutaneous metastasis are found in about 22% of patients. [16, 17]

Tumors measuring greater than 1 cm have been reported to have twice the mortality rate of lesions measuring less than 1 cm. Due to its clinical behavior, the recommended treatment for moderately differentiated neuroendocrine carcinomas is radical surgical resection. [16, 17]

Partial or total laryngectomy my be performed depending on the site and extent of the primary tumor. As most tumors are supraglottic in location, supraglottic laryngectomy is often the procedure of choice. [1]

Elective neck dissection appears to be warranted in view of the high incidence of both early cervical metastasis and subsequent involvement of cervical nodes. The dissection of sublevel IIA and level III only is adequate for elective surgical treatment of the neck in supraglottic and glottic tumors. [1]

Conclusion

Neuroendocrine carcinomas are very infrequent and aggressive, which is why early and accurate diagnosis is essential, as well as their classification, since the prognosis and treatment depend on the variety of neuroendocrine carcinoma, this is where immunohistochemistry becomes important, since A well-differentiated tumor could be treated with conservative surgical treatments and without neck dissection, and patients with less differentiation require more radical surgeries, in our case the patient with a moderately differentiated variety, responded well to conservative treatment, with excisional biopsy and application of radiotherapy. Currently, the presence of disease has not been identified in the PET / CT controls. As these are rare tumors, the existing cases are few and the treatments are not standardized, which is why more randomized studies are required.

Conflicts of interests

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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