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Adenosquamous carcinoma of the larynx: impact of the unusual phenotype on definitive treatment. A case report.

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Abstract: The malignant laryngeal tumors include a variety of histological types with different biological characteristics, and therefore require a different therapeutic approach and lead to a variety of prognosis. Clinical case: we present a case of adenosquamous carcinoma of the larynx, in a 57-year-old male patient who, since July 2016, has presented progressive dysphonia. He goes to a foreign doctor, who evaluates him and performs nasofibrolaryngoscopy, evidencing glottis tumor, and refers to this center. He is evaluated and direct laryngoscopy plus biopsy is performed, classified as cT3N1M0 stage III, total laryngectomy plus bilateral modified radical cervical dissection is performed in 2017, subsequently referred to the radiotherapy and medical oncology service, and he receives adjuvant concurrent chemo radiation therapy, the patient remains disease free to the date. Discusion: it is an extremely rare neoplasm, whose histological characterization is distinctive, due to the presence of mixed areas of unequivocal adenocarcinoma and the squamous cell carcinoma. The combined surgery and the additional adjuvant radiotherapy found to be necessary because the biological behavior and prognosis of this neoplasm considered more aggressive than those of conventional squamous cell carcinoma are. There is no standardized treatment; it based on the possibility of the surgical resection, whose extension resulted from tumor infiltration into the adjacent structures, followed by concurrent radiotherapy or chemo-radiation therapy.

Key words: cancer; larynx adenosquamous; head and neck; surgery; radiotherapy; chemotherapy

1 Introduction

Laryngeal cancer accounts for 0.25% of all cancer cases worldwide in 2020 [1]. Ninety percent of these cases are squamous cell carcinomas [2]. The incidence rate increases with age, being considerably higher after the age of 50, and is more prevalent in men, with a ratio of 7:1 compared to women [1]. In countries such as the US, approximately 12,000 new cases of laryngeal cancer are diagnosed each year, resulting in 4,000 deaths per year [3]. In Venezuela, laryngeal cancer ranks 18th in terms of incidence and estimated mortality according to Globocan 2020, with 1.3% of new cases, 1.5% mortality, and a 5-year survival rate of 7.16/100,000 inhabitants. The main risk factors are tobacco and alcohol consumption [4], but genetic factors [5] and human papillomavirus infection [6,7] have also been described. The glottis is the most common location (65%), followed by the supraglottis (34%) and subglottis (1%) [8]. However, some literature uses the "transglottic" classification to refer to extensive carcinomas that cross the laryngeal ventricle and extend into the paraglottic space and subglottis, making it difficult to define their origin [4,9,10]. The TNM classification of the American

Joint Committee on Cancer (AJCC) is used for staging, which is specific to each site in the larynx [11]. However, there are characteristics common to all sites, such as vocal cord fixation and invasion of the thyroid cartilage, which correspond to T3 and T4, respectively [11]. Laryngeal cancer is usually diagnosed when it is already advanced, corresponding to stages III and IV [12]. In terms of treatment, advanced stage (T4) laryngeal cancer is treated with total laryngectomy, which may be associated with postoperative adjuvant radio-chemotherapy [12]. According to foreign studies, this pathology has a five-year survival rate of between 73% and 92% in the early stages and 50% to 64% in the late stages [4].

Laryngeal adenosquamous carcinoma accounts for 0.5% to 1% of squamous cell carcinoma subtypes in this organ. Less than 100 cases have been reported in the international literature [13]. It is a biphasic tumor characterized by malignant proliferation of squamous and glandular components. Its origin is due to the divergent differentiation of the most basal cells of the epithelium [14]. The clinical presentation is indistinguishable from classic laryngeal squamous cell carcinoma, debuting with dysphonia, dyspnea, and dysphagia in large tumors. It is predominant in men between the sixth and seventh decades of life. Regional and distant spread is characteristic, reaching up to 75% and 25% respectively [15]. Its infrequent presentation limits the establishment of standardized treatment protocols; however, given the aggressive course of the disease, it is advisable to aggressive surgical treatment as a fundamental pillar, followed by adjuvant treatment, given by radiotherapy or concurrent chemoradiotherapy [16,17] .

In Venezuela, there is no current registry of the incidence of cases nor reports of this histological type, attributable to its overall low incidence, with little information available worldwide and in our country. Therefore, we consider it important to present this case to the community, along with its initial and definitive management.

2 Clinical case

A 57-year-old male, hypertensive and controlled type 2 diabetic, heavy smoker, pack-year index (PYI) of 32 packs/year, frequent alcohol consumption without reaching intoxication, family history of cancer with father deceased from laryngeal cancer and brother deceased from lung cancer, who reported onset of current illness in July 2016 with progressive dysphonia, for which he decided to see a specialist in September 2016. The physician performed a nasofibrolaryngoscopy, revealing a glottic tumor, and decided to refer him to this center.

The patient was evaluated in the consultation area, and a computed tomography (CT) scan of the neck and chest was requested (Figures 1 and 2), which showed partial obliteration of the laryngeal lumen, without erosion of the cartilage, as well as bilateral cervical lymph nodes smaller than 1 cm, and extensive bullous disease in the chest, predominantly in the upper lobes, without nodular lesions suggestive of secondary extension. A decision was made to perform direct laryngoscopy and biopsy in the surgical area, where findings revealed an exophytic, friable tumor occupying the left vocal cord with infiltration of both arytenoid-epiglottic folds.

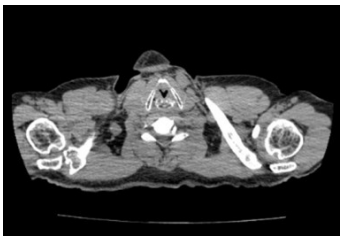

Figure 1. Neck CT scan

Figure 2. Chest CT

The biopsy results are subsequently received, reporting a malignant epithelial neoplasm with a squamous predominance (80%), together with islands of incomplete glandular differentiation, infiltrating the stroma (Figures 3 and 4, blue arrow and ovals).

The patient was diagnosed with cT3N1M0 stage III adenosquamous carcinoma of the larynx, and it was decided to perform a total laryngectomy plus bilateral modified radical neck dissection. The surgical specimen was evaluated by pathological anatomy and was consistent with the initial histopathological diagnosis, reporting negative margins and sixteen lymph nodes in total, free of neoplasia (Figure 5), for which the definitive diagnosis is corrected to: laryngeal adenosquamous carcinoma pT3N0M0 stage III.

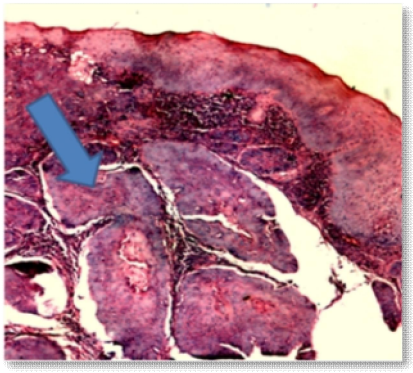

Figure 3. Direct laryngoscopy specimens (H-E)

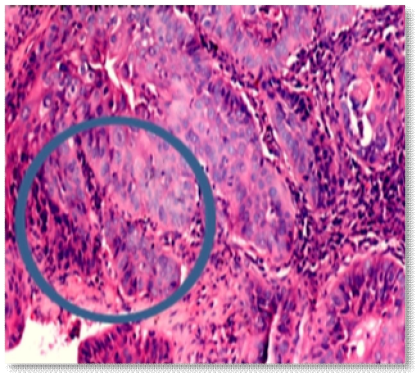

Figure 4. Total laryngectomy specimen (H&E)

The case is discussed at a head and neck service meeting, and it is decided to refer the patient to the radiotherapy service. The patient undergoes adjuvant radiotherapy with a total dose of 6,120 cGy and is currently disease-free.

3 Discussion

The diagnosis of laryngeal cancer with unusual histology has become a challenge for specialists. According to

reported cases of laryngeal carcinomas, dysphonia is the first sign to manifest, according to Pradenas et al. [18] as well as Sotomayo et al. [5] , who found in their retrospective study that dysphonia was present in more than 90% of cases. In our setting, delayed consultation represents the biggest problem for these patients, attributed to the patient's refusal to attend, lack of knowledge among the population or even among primary health care professionals about identifying chronic dysphonia as a symptom that could be caused by laryngeal cancer, especially in patients with risk factors such as tobacco and alcohol consumption [5].

One of the important risk factors present in this case is the smoking habit in correlation with alcohol consumption. The relationship between smoking and the appearance of tumors with unusual histology is not described in the literature as significant. However, it is a common habit in patients with laryngeal carcinoma in general, as in our case [19].

In relation to the location of the tumor, those that exclusively involve the subglottis tend to have unusual histology. Contreras et al. described 43 patients with squamous cell carcinoma of the larynx, none had lesions only in the subglottis [4]. Of the five patients reported in this publication, two had subglottic locations—one case of chondrosarcoma and one of adenoid cystic carcinoma, respectively. For both tumors, the subglottic location is the most frequently described [4, 8].

Consequently, we can consider that adenosquamous carcinomas, which are extremely rare histologically in terms of their incidence, should be suspected on a statistical basis in patients under 60 years of age and with subglottic location. In addition, it should be considered in female patients who are non-smokers and when the histological diagnosis requires more than one biopsy sample.

In the treatment and management of these patients, the literature describes the main modalities, which are: radiotherapy and concurrent chemoradiation. In a study conducted by Sotomayor et al. [4], adjuvant treatment in their total population consisted of radiotherapy or chemoradiotherapy in 63.79% of the 174 patients who underwent curative-intent treatment, while total laryngectomy was performed in 28.73%. An absence of adjuvant treatment was reported in 30.6% of patients undergoing total laryngectomy, which may be linked to the absence of an oncology committee during the early years studied in this research. Along these lines, it has been reported that approximately 60% of T3 and T4 patients who receive surgical treatment should undergo adjuvant radiotherapy [16,20] , and this figure should reach 100% in patients with T4 carcinoma. Although this study did not show a significant difference in survival curves between patients who received postoperative adjuvant therapy before and after 8 weeks, this could be associated with the small size of the subgroup that received adjuvant therapy (33 patients). They report overall survival rates of 86.6% at 2 years and 77.4% at 5 years for patients in early stages; and 45.2% at 2 years and 33% at 5 years for advanced stages [4]. This is consistent with other studies conducted in the US by Wolf et al. [17].

We conclude that:

1. Adenosquamous laryngeal carcinoma is rare and its diagnosis is primarily pathological, since the clinical presentation, imaging studies, and macroscopic findings do not differ from other histologies of laryngeal carcinoma.

2. There is no standardized treatment; however, the therapeutic trend is based mainly on surgical treatment, the extent of which will depend on tumor infiltration into adjacent structures, followed by radiotherapy or concurrent chemoradiotherapy.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] World Health Organization (WHO). GLOBOCAN, International Agency for Research on Cancer (IARC), 2020. Disponible en: URL: https://www.uicc.org/news/globocan-2020-new-global-cancer-data.

[2] Luers J, Sircar K, Drebber U, Beutner D. The impact of laryngeal dysplasia on the development of laryngeal squamous cell carcinoma. Eur Arch Otorhinolaryngol. 2014;271(3):539-545.

[3] Cardemil F, Ortega G, Cabezas L. Importancia de la epidemiología en cáncer laríngeo: Incidencia y mortalidad por carcinoma escamoso de laringe. Rev Otorrinolaringol Cir Cabeza Cuello. 2017;77(1):107-112.

[4] Sotomayor JD, Cabezas CL, Fernández LA, Schuller FM, Torrejón W, Papuzinski AC. Supervivencia de carcinoma escamoso de laringe en Hospital Carlos Van Buren. Rev. Otorrinolaringol Cir Cabeza Cuello. 2020;80(3):286-294.

[5] Conway DI, Hashibe M, Boffetta P, INHANCE consortium, Wunsch-Filho V, Muscat J, et al. Enhancing epidemiologic research on head and neck cancer: INHANCE - Thee international head and neck cancer epidemiology consortium. Oral Oncol. 2009;45(9):743-746.

[6] IARC Working Group on the evaluation of carcinogenic risks to humans. Human papillomaviruses. IARC Monogr Eval Carcinog Risks Hum. 2007;90:1-636.

[7] Mehanna H, Jones T, Gregoire V, Ang K. Oropharyngeal carcinoma related to human papillomavirus. BMJ. 2010;340:c1439.

[8] Nocioni R, Molteni G, Mattiuzi C, Lippi G. Updates on larynx cancer epidemiology. Chin J Cancer Res. 2020;32(1):18-25.

[9] Orellana M, Chuang A, Fulle A, Fernández R, Loyola F, Imarai C. Cáncer de laringe: serie de casos en 6 años en el Complejo Asistencial Doctor Sótero del Río. Rev Otorrinolaringol Cir Cabeza Cuello. 2017;77(1):35-43.

[10] Contreras P, Muñoz D, Contreras J, Rahal M. Momento de inicio de radioterapia posoperatoria como factor pronóstico en pacientes con cáncer de laringe avanzado. Rev Otorrinolaringol Cir Cabeza Cuello. 2018;78:406-412.

[11]Amin M, Edge S, Greene F, Compton C, Gershenwald J, Brookland R, et al. AJCC Cancer Staging Manual. 8. edición. Nueva York: Springer International Publishing; 2017.

[12] Steuer C, El-Deiry M, Parks J, Higgins K, Saba NF. An Update on larynx cancer. CA Cancer J Clin. 2017;67(1):31-50. https://doi.org/10.3322/ caac.21386.

[13] Dubal PM, Unsal AA, Echanique KA, Vazquez A, Reder LS, Baredes S, et al. Laryngeal adenosquamous carcinoma: A population-based perspective. Laryngoscope. 2016;126:858-863.

[14] Gale N, Zidar N, Cardesa A, Nadal A. Benign and potentially malignant lesions of the squamous epithelium and squamous cell carcinoma. En: Cardesa A, Slootweg PJ, Gale, Franchi A, editores. Pathology of the head and neck. Berlin: Springer;2016. p.1-48.

[15] Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-E386. doi: 10.1002/ijc.29210.

[16] Graboyes E, Zhan K, Garrett-Mayer E, Lentsch E, Sharma A, Day T. Effect of Postoperative radiotherapy on survival for surgically managed pT3N0 and pT4aN0 laryngeal cancer: Analysis of the National Cancer Data Base. Cancer. 2017;123:2248-2257. https://doi.org/10.1002/cncr.30586.

[17] Wolf GT, Bellile E, Eisbruch A, Urba S, Bradford CR, Peterson L, et al. Survival rates using individualized bioselection treatment methods in patients with advanced laryngeal cancer. JAMA Otolaryngol Head Neck Surg. 2017;143:355-366.

[18] Pradenas M, Vallejos M, Rahal M, Cisternas A. Cáncer de laringe e hipofaringe. Experiencia del Hospital Barros Luco Trudeau 1990-2001. Rev Otorrinolaringol Cir Cabeza Cuello. 2004;64:13-20.

[19] Passon P, Tessitori G, Lombardo M, Callea S, Poli, P. Long-surviving case of adenosquamous carcinoma of the larynx: Case report and review of literature. Acta Otorhinolaryngologica Italica. 2005;25(5):301-303.

[20] Skóra T, Nowak-Sadzikowska J, Mucha-Malecka A, Szyszka-Charewicz B, Jakubowicz J, Glinski B. Postoperative irradiation in patients with pT3-4N0 laryngeal cancer: Results and prognostic factors. Eur Arch Otorhinolaryngol. 2015;272(3):673-679.