4. Lewis JE, Olsen KD, Sebo TJ. *Spindle cell carcinoma of the larynx: Review of 26 cases including DNA content and immunohistochemistry* Hum Pathol 1997; 28: 664-673.
5. Lane N. *Pseudosarcoma (polypoid sarcoma-like masses) associated with squamous cell carcinoma of* the *mouth, tauces and larynx. Report ot10 cases.* Cancer 1957; 10:19-41.
6. Ackerman LV. *Verrucous carcinoma ofthe oral cavity* Surgery 1948; 23: 670-678.
7. Biller HF, Ogura JH, Bauer WC. *Verrucous cancer of the larynx.* Laryngoscope 1971; 81:1323-1329.
8. Orvidas LJ, Olsen KD, Lewis JE et al. *Verrucous carcinoma of the larynx: A review of53 patients.* Head Neck 1998; 20: 197-203.
g. Spiro RH. *Verrucouscarcinoma, then and now* Am JSurg 1998; 176: 393-397.
10. Michaels L. *Unusual lorms ot squamous cell carcinoma: Spindle cell carcinoma, verrucous squamous carcinoma, ventriculosaccular carcinoma.* In: Ear, Nose and Throat Histopathology. Springer-Verleg, Berlin, Heidelberg 1987; 405-419.
11. Cooper JR, Hellquist HB, Michaels L. *Image analysis in the discrimination ot verrucous carcinoma and squamous papilloma.* J Pathol 1992; 166: 383-387.
12. Multhaupt HA, Fessler JN, Warhol MJ. *Detection ot human papillomavirus in laryngeal lesions by in situ hybridization.* Hum Pathol 1994; 25: 1302-1305.
13. Wain SL, Kier R, Vollmer RT et al. *Basaloid-squamous carcinoma of the tongue, hypopharynx, and larynx: Report of ten cases.* Hum Pathol 1986; 17: 1158-1166.
14. Hellquist HB, Dahl F, Karlsson MG et al. *Basaloid squamous cell carcinoma of the palate.* Histopathology 1994; 25: 178-1 80.
15. Ferlito A. *Unusual forms of squamous cell carcinoma.* In: Ferlito A. (Ed.). Surgical Pathology ot Laryngeal Neoplasms. Chapman & Hall, London 1996; 143-171.
16. Banks ER, Frierson HF Jr, Mills SE et al. *Basaloid squamous cell carcinoma of the head and neck. A clinicopathologic and immunohistochemical study of 40 cases.* Am J Surg Pathol 1992; 16: 939-946.
17. Morice WG, Ferreiro JA. *Distinction ofbasaloid squamous cell carcinoma from adenoid cystic and small cell undifferentiated carcinoma by immunohistochemistry.* Hum Pathol 1998; 29: 609-612.

Adenocarcinomas and salivary gland neoplasms of the larynx

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Introduction

Minor salivary gland tumors of the larynx are rare; only a few large series have been reported from a single institution. Therefore, details of their clinical and pathological behavior come only through composite analysis of small series. Less than 1% of the epithelial malignancies of the larynx are of salivary gland origin.

Subepithelial and intraepithelial glands

The sites of origin of the salivary gland neoplasms of the larynx follow the anatomical distribution of the larynx subepithelial glands and the intraepithelial mucous glands. Approximately two-thirds of the adenoid cystic carcinomas are in the subglottis, The other carcinomas, in contrast, are rarely subglottic, with supraglottic and transglottic involvement being nearly equal. The lower part of the glottic region shows the greatest differences in density of submucosal glands: 13 glands/cm2 on the vocal cords to 128 glands/cm2 on the false vocal cords and medial wall of Morgagni's sinus. The greatest concentration of glands is in the saccule (139 glands/cm^2). There is a Very low density of glands in the extrinsic laryngeal regions. A typical intraepithelial gland is made up of 15-30 mucus-secreting cells with a structure like that of goblet cells. They extend from the epithelial surface down toward the basement membrane, on which they may rest, but do not penetrate. Irregularly distributed in the larynx, intraepithelial glands are most numerous in the supraglottis and least numerous in the subglottis.

Salivary gland neoplasms

With the exception of adenoid cystic carcinomas, salivary-type carcinomas are rare in the larynx. Even pleomorphic adenomas are almost curiosities in this organ.

Benign neoplasms

Benign laryngeal neoplasms are extremely unusual with exception of oncocytic lesions.

Oncocytic lesions (metaplasia, hyperplasia, oncocytoma

Oncocytic lesions of the larynx occur most often in patients aged 50-80 years. A slight predominance of male patients exists. These lesions are most often located in the false Vocal cord or laryngeal ventricle areas. The microscopic findings in most cases suggest oncocytic metaplasia and cystic hyperplasia rather than neoplasia. Well-defined, columnar, oncocytic epithelium arises from seromucous ducts or acini and subsequently expands into cystic structures. Papillary growths into the cystic spaces are common. The process seems to be multifocal in the large majority of cases, and this contributes to the impression that this is a metaplastic process.

Pleomorphic adenoma

Certainly, the diagnosis of pleomorphic adenoma in this anatomic location should be entertained cautiously, and distinction from the many tumors that occur more frequently *(e.g.,* adenoid cystic carcinomas, mucoepidermoid carcinoma and low-grade chondrosarcoma) should be foremost in the mind of the pathologist.

Other benign tumors

Myoepitheliomas have been rarely reported in the larynx. The morphology and clinical course has been identical to their counter part in the major salivary glands.

Malignant neoplasms

Adenoid cystic carcinomas

Adenoid cystic carcinomas of the larynx comprise only about 0.25% of laryngeal carcinomas. The age range of occurrence is fairly wide, but they are found most often in the fourth to the sixth decades of life. The sex incidence is approximately equal. These laryngeal tumors most often occur in the subglottic area, but a substantial proportion are found supraglottically, Tumors of glottic origin are even less common. The histological features are the same as those seen with adenoid cystic carcinomas found at other sites. Total laryngectomy has generally been employed for treatment. Not unexpectedly, a high incidence (>50%) of local treatment failure does occur; thus postoperative radiotherapy may be beneficial. Because the reported incidence of lymph node metastasis is higher than that for adenoid cystic carcinomas elsewhere, some have recommended elective neck dissection.

Mucoepidermoid carcinoma

The presenting signs and symptoms of laryngeal mucoepidermoid carcinomas mimic those of squamous cell carcinoma of the larynx. Hoarseness is common and some patients have hemoptysis, foreign body sensation, dysphagia, or a neck mass. Reported lesions have varied in size from about 0.5-5.0 cm. Nothing in their gross appearance distinguishes them from squamous cell carcinomas. Microscopically, low-grade mucoepidermoid carcinomas of the larynx resemble the same type of tumor found in other sites, and recognition is usually not too difficult. High-grade mucoepidermoid carcinomas may resemble poorly differentiated squamous cell carcinomas. The behavior of these laryngeal tumors has been referred to as unpredictable. This may partly result from analyses that contain different numbers of high-grade adenosquamous carcinomas, which often are difficult to separate from mucoepidermoid carcinomas. Although histological grading influences treatment, the most important factor in therapy is the clinical stage. Total laryngectomy has been the most frequently employed treatment, but appropriately small or limited lesions have been treated with vertical hemilaryngectomy or supraglottic laryngectomy, In the presence of clinically enlarged neck lymph nodes, neck dissection should generally be performed. On the basic of our own experience and that of the Armed Forces Institute of Pathology, it is safe to presume that except for low-grade mucoepidermoid carcinomas, other supposed grades of that carcinoma in the larynx are much more likely to be adenosquamous carcinomas.

Adenospuamous carcinoma

This highly malignant neoplasm may arise from overlying surface mucous or from the ducts of minor salivary glands. Microscopically, adenocarcinomatous and squamous carcinomatous components should be present in a single neoplasm with intercellular bridges or keratin demonstrable in the squamous component. Approximately 40 cases have been reported in the larynx. However, the diagnostic criteria are not universally accepted, and some authors do not distinguish between adenosquamous and high-grade mucoepidermoid carcinoma. Furthermore, whether primary adenosquamous carcinoma of the minor salivary glands exists is controversial, most authors consider this carcinoma of surface origin.

Adenocarcinomas

There is also a frustrating lack of clarity in what constitutes an "adenocarcinoma" of the larynx affer exclusion of adenoid cystic carcinoma. From the literature one gets the distinct impression that the so-called adenocarcinomas are poorly differentiated, large, bulky, and preponderantly supraglottic neoplasms that are subsurface in origin. When photomicrographic illustrations are available, many, if not most, have a neuroendocrine appearance.

Miscellaneous carcinomas

A few cases of laryngeal acinic cell carcinoma have been reported in the literature. Epithelia-myoepithelial carcinoma, myoepithelial carcinoma, carcinoma expleomorphic adenoma and salivary duct carcinoma have also been reported to occur in the larynx.

References

- Bak-Pedesen K, Nielsen KO. *Subepithelial mucous glands in the adult human larynx. Studies on number, distribution and density* Acts Otolaryngol 1986; 102: 341-352.
- Baptists PM, García-Tapia R, Vázquez JJ. *Pleomorphic adenoma of the epiglottis.* J Otolaryngol 1992; 21: 355-357.
- Della-Palma P, Blandamura S. *Clear cell carcinoma of the larynx: Immunocytochemical study* Tumori 1989; 75: 594-596.
- Damiani JM, Daminani KK, Heuck K et el. *Mucoepidermoid-adenosquamous carcinoma of the larynx: A report of 21 cases and review of the literature.* Otolaryngol Heed Neck Surg 1981; 89: 235-243.
- Ferlito A, Gale N, Hvala H. *Laryngeal salivary duct carcinoma. A light and electron microscopic study* J Leryngol Otol 1981; 95: 731-738.
- Ibrahim R, Bird DJ, Sieler MW. *Malignant myoepithelioma of the larynx with massive metastatic spread to the liver: An ultrastructural and immunocytochemical study* ultrastruct Pathol 1991; 15: 69-76.
- Kallis 5, stevens DJ. *Acinous cell carcinoma of the larynx.* J Laryngol Otol 1989; 103: 638-641.
- Latjman Z, Vranesic D, Krpen D. *Oncocytic lesions of the larynx.* Lilec Vjesn 1993; 15: 42-45.
- Lipport PM, Werner JA, Schluter E et al. *Mucoepidermoid cancer of the larynx. Case report and review of the literature.* Laryngorhinootologie 1992; 71: 495-499.
- Lundgen J, Olofsson J, Hellquest H. *Oncocytic lesions of the larynx.* Acts Otolaryngol 1982; 94: 335-344.
- Martinez-Madrigal F, Baden E, Gasireghi O et al. *Oral and pharyngeal adenosquamous carcinoma. Report of four cases with immunohistochemical studies.* Eur Arch Otorhinolaryngeal 1991; 248: 255-258.
- Martinez-Madrigal F, Sentiago-Payen H, Meneses A. *Plasmacytoid myoepithelioma of the laryngeal region: A case report.* Hum Pathol 1995; 26: 802-804.
- Mikaelian DO, Contrucci RB, Batsakis JG, *Epithelial myoepithelial carcinoma of the subglottic region: A case presentation and review of the literature.* Otolaryngol Head Neck Surg 1986; 95:108-106.
- Mildford CA, Mugliston TA, O'Flynn P et el. *Carcinoma arising in a pleomorphic adenoma of the epiglottis.* J Laryngol Otol 1989; 103: 327-327.
- Pignataro L, Brambille D, Scotti A. *Carcinoma adenoideo cistico delta laringe e dell'ipofaringe. Relazione su di un caso clinico e revisione dells lefteratura.* Otorinolaringologie. 1991; 41:141-144.
- Spiro RH, Lewis JS, Hajdu SI et el. *Mucus gland tumors of the larynx and laryngopharynx.* Ann Otol Rhinol Laryngol 1976; 85: 498-503.

Gene alterations in precancerous and cancerous lesions of the larynx

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Stratified squamous epithelium is composed of several layers with distinct biological functions, Cells in the basal layer, which make contact with basal membrane, are stem cells with the ability to proliferate and provide new elements for the upper layers. However, the main proliferative activity is detected by Ki67 expression in cells located immediately above them, Going upwards, the prickle cell layer is the most populated, as well as the most morphologically characteristic. These cells are still metabolically active, their main function being the production of keratin. Cells that enter the prickle cell layer express p21WAF1 instead of Ki67, but this expression is transitory because it is seen only in the lower layers (1).

Appropriate mechanisms regulating cell growth and differentiation maintain the normal turnover that controls epithelial thickness, perhaps through cyclin-dependent kinase inhibitors (OKIs), such as p21WAF1. It is widely accepted that malignant transformation of squamous epithelium progresses through a number of steps, some of which can be morphologically recognized, such as the so-called