

## MINI-REVIEW

# SPECIFIC DIAGNOSTIC ASPECTS IN BENIGN LARYNGEAL TUMORS – MINI REVIEW

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### ABSTRACT

Benign laryngeal tumors represent a wide range of lesions with a high histological variety, nonspecific symptomatology such as dysphonia, which equally affects both genders and in some cases may evolve to important complications, with functional consequences or malignisation, in the absence of a proper therapeutic attitude. Authors aim to review the main benign tumors of the larynx, according to the histological type, by presenting particular lesions aspect, in order to establish a diagnosis which will be certified by the histopathological exam.

**Key words:** benign tumors, larynx, histopathological exam.

### RÉSUMÉ

**Aspects diagnostiques spécifiques des tumeurs bénignes du larynx**

Les tumeurs bénignes à localisation laryngée sont des lésions présentant une importante variété histologique, sans symptomatologie clinique spécifique, mais dominée essentiellement par la dysphonie, affectant en proportions approximativement équivalentes les deux sexes. Elles peuvent évoluer dans certains cas vers des complications redoutables sur le plan fonctionnel, voire subir une transformation maligne en l'absence d'une thérapie appropriée et rapidement mise en pratique.

Les auteurs cherchent à passer en revue les principales affections tumorales bénignes du larynx en fonction de leur type histologique, en présentant leurs particularités à l'analyse anatomo-pathologique, afin que celle-ci permette d'établir un diagnostic précis et de certitude.

**Mots clefs:** tumeurs bénignes, larynx, examen histopathologique

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## INTRODUCTION

The benign tumors encountered at the level of the larynx show a great variability, from histological to location site of appearance<sup>1</sup>.

Depending on the histological type, these tumors can be classified in:

- Epithelial tumors
  - Squamous epithelium tumors (recurrent respiratory papillomatosis, keratinised papilloma);
  - Glandular tumors (pleomorphic adenoma, oncocytic tumor).
- Non-epithelial tumors
  - Vascular tumors (haemangioma, lymphangioma);
  - Cartilage and bone tumors (chondroma, osteoma, giant cell tumor);
  - Muscle tumors (leiomyoma, rhabdomyoma, angiomyoma, epithelioid leiomyoma);
  - Adipose tumors (lipoma);
  - Neural tumors (neurilemmoma, neurofibroma, schwannoma, paraganglioma, granular cell);
  - Pseudotumors (fibroma, inflammatory fibroblastic, amyloid, laryngeal cysts)<sup>1</sup>.

The diagnosis of these lesions is based on a thorough medical history, with focus on the main signs and symptoms, their appearance and evolution, performing specific and nonspecific laboratory tests (indirect laryngoscopy, laryngeal videoendoscopy, videostroboscopy), sometimes imaging tests (CT scan, MRI scan), histopathological examination and sometimes immunohistochemical tests. The clinical presentation of these tumors is closely related to the location and size of the lesions. They frequently present a slow evolution, with insidious onset of symptoms. The main symptoms are represented by dysphonia, dyspnea and dysphagia<sup>1</sup>. In most of the cases, surgical treatment is achieved through microlaryngoscopy<sup>2</sup>.

The authors aim to present the main forms of benign laryngeal tumors, with focus on the individual items required to diagnose them.

Laryngeal papilloma is a benign tumor that affects the squamous epithelia of the larynx. Barnes divides these tumors in 2 types: keratinized and non-keratinized<sup>3</sup>. The keratinized papilloma usually appears in adulthood, at the site of the vocal cords, isolated, being associated with smoking. and presents a significant risk of malignant transformation. The non-keratinized papilloma has a viral etiology and it is usually found at younger ages. The illness is severe due to its recurrent and expansive character. The virus associated with laryngeal papillomatosis is part of the PAPOVA virus group and the most frequent viral subtypes are 6 and 11<sup>3</sup>. Subtype 6 is found in

the forms of disease that affect adults. The papilloma virus infection determines dysfunctions of the laryngeal mucosa, by altering the cytokeratin and the surface carbohydrates<sup>4</sup>.

The most severe form of illness is caused by subtype 11 of the human papillomatosis virus, due to frequent recurrences and the extension of lesions that characterize it. In children, this is revealed by dysphonia, shortness of breath and an increased respiratory rate. In severe forms, the patient is admitted with acute respiratory failure, therefore necessitating a tracheostomy.

Macroscopically, the papilloma presents itself as an exophytic pink-reddish or whitish mass, pedicled, localized on the vocal cords. It can also be found in the trachea, the bronchi, the hard palate, the soft palate, the nasopharynx and the pulmonary parenchyma<sup>3</sup>. There have been described cases in which the lesions are multiple and confluent and the entire larynx has a tumor-like aspect (Figure 1).

Vocal nodules have been illustrated for the first time by Turck in 1866, under the denomination of chorditis tuberosa. Nowadays, they are described as mucosal thickenings localized bilaterally on the free margins of the vocal cords, at the union of the middle and anterior thirds. The patient is admitted with persistent dysphonia of variable severity, stinging sensations, muscle aches, vocal deficiency, laryngeal dryness in phonation. As a result, the patient's voice is perceived as deficient, unpleasant and, therefore, he voluntarily tries to change it<sup>5</sup>. Indirect laryngoscopy reveals a nodular mass of variable size, uni- or bilateral, localized on the free margins of the vocal cords, between the middle and anterior thirds (Figure 2).

The vocal nodules can present in several forms:

- spiny nodule - a firm, whitish ear covered by mucus;
- edematous nodule - a smooth, soft and pale mass;
- fibrous nodule - bigger, tougher and with a rough surface;
- nodosity - a large nodule (3-4 mm), that appears mostly in children;
- kissing - nodules or the hemangioma nodule - appears from a sanguine fusion, as an outcome of a trauma of the vocal cords at the nodular point. They are described as a round, red, smooth pearl, uneven in size.

The laryngeal polyp, first described by Czermak in 1859, is represented by a benign tumor on the vocal cords, as a result of an inflammatory process at this level. It usually affects people with ages between 30-50 years old, who had suffered an acute or chronic vocal injury. The first symptoms are represented by: vocal impairment of sudden appearance or

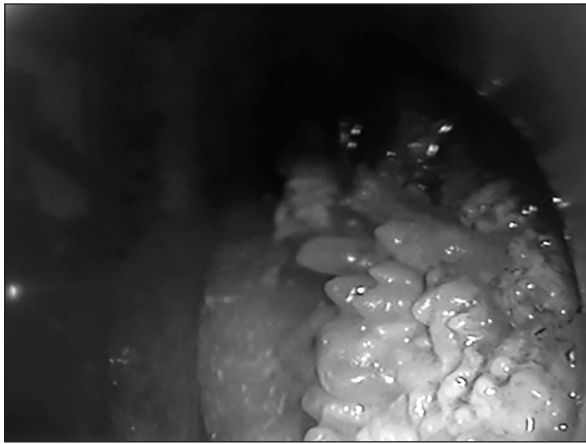


Figure 1. Laryngeal papilloma of the larynx

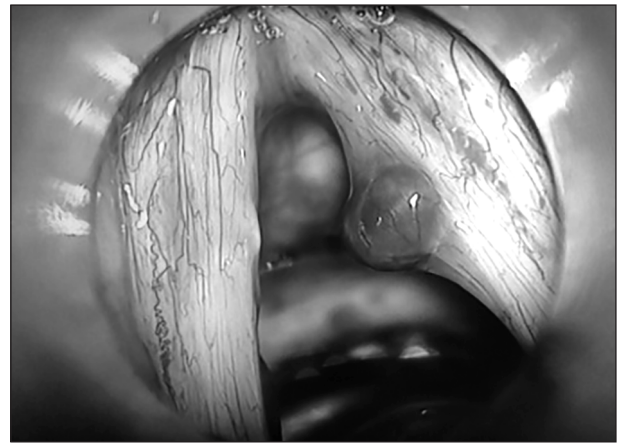


Figure 3. Laryngeal polyp of right vocal fold

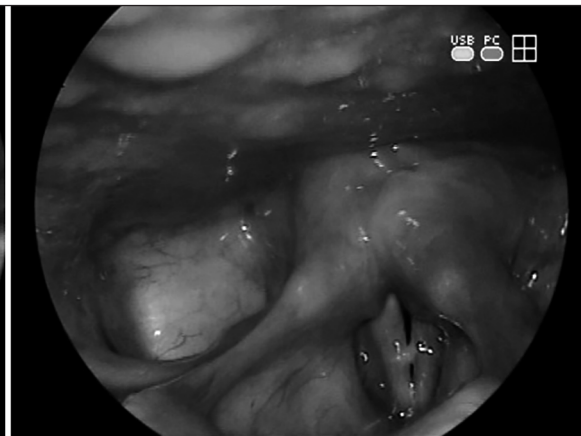


Figure 2. Vocal nodules – endoscopic view

dysphonia, that isn't decreased through medication, but it progresses; irritating dry cough; foreign body sensation. Depending on the localization of the lesion and the type of insertion, the patient's voice may sometimes be bitonal<sup>5</sup>.

Indirect laryngoscopy reveals a round mass of variable size, frequently unique, sessile or pedicled, usually localized on the anterior third of the vocal cord (Figure 3). The mobility of the vocal cord isn't affected. Sometimes, these nodules can be hemorrhagic or edematous<sup>3</sup>.

The adenoma originates in the mucous glands of the larynx. It is a rare benign tumor, predominant in males, being situated at the site of the ventricular bands and the Morgagni ventricle. The most significant symptoms are dysphonia and shortness of breath. Occasionally, this tumor is randomly discovered during an ENT examination. The gold standard for diagnosis is the histopathological exam<sup>3</sup>.

The laryngeal angioma represents a benign tumor, with an incidence of less than 1% of all the benign lesions discovered at this site. It is divided in

2 types: pediatric and adult angioma. This lesion is most frequently discovered in the subglottis, although there have been described cases with appearances in the vocal cords or the pyriform sinuses. Clinically, the patient complains of dysphonia. The indirect laryngoscopy reveals a smooth, pedicled tumor, which is well delimited and reddish<sup>3</sup>. The biopsy is contraindicated due to the high risk of hemorrhage that may endanger the patient.

The chondroma is a rare benign cartilaginous tumor, encapsulated, originating from the cricoid cartilage (70% of the cases), from the thyroid cartilage (20% of the appearances) or from the epiglottis and the arytenoid cartilages (10% of the sites). It appears in the 6<sup>th</sup>-7<sup>th</sup> decades, with symptoms which include progressive dysphonia, shortness of breath, dysphagia and stridor<sup>6</sup>. The tumor is described as well delimited, with a wide base of insertion, covered by unmodified endolaryngeal mucosa.

The laryngeal lipoma represents 13% of the benign tumors of the fatty tissue discovered in the neck and head<sup>7</sup>. Depending on the lesion's localization, the

symptoms vary from dysphonia, shortness of breath, dysphagia. An indirect laryngoscopy reveals a sessile or pedicled formation, frequently localized/situated at the site of the aryepiglottic folds, the epiglottis or the vocal cords. The pedicled tumors may lead to severe shortness of breath with acute respiratory distress.

The tumors that originate from the laryngeal nervous system are pretty rare at this level. Clinically, the patient complains of persistent dysphonia in different stages of severity. The diagnosis of certitude is based on the histopathological examination which also classifies the tumor.

The neurofibroma derives from the nervous sheath and has a low laryngeal incidence. The symptoms include dysphonia and shortness of breath. The laryngeal endoscopic examination reveals a firm, pink or yellowish formation, localized at the site of the aryepiglottic folds. Sometimes, the lesions may be multiple and of variable sizes<sup>3</sup>.

The schwannoma originates from the Schwann cells. The most frequent site is the laryngeal vestibule. The size of the tumor determines the severity of the symptoms, which include dysphonia, foreign-body sensation, pain. The lesion's full assessment requires a MRI and a CT examination in order to differentiate the tumor from the laryngeal soft tissues.

The myoblastoma or the granular cell tumor originates from the Schwann cells, therefore it can be localized anywhere in the human body<sup>6</sup>. 50% of the cases present a tumor situated in the head and neck and 10% of these in the larynx. Clinical manifestations include persistent dysphonia, sometimes associated with irritating cough. The laryngoscopic examination reveals a small, nodular, white-grey formation, covered by normal mucosa, which is situated on the posterior end of the vocal cords<sup>3</sup>.

Paraganglioma is a rare neuroendocrine tumor, originated from the site of the neural crests. It is characterized by a slow growth and it is frequently discovered in female gender, mostly on the right side, on the ventricular bands and/or the aryepiglottic folds. Fibroscopy reveals a cystic mass, reddish or bluish in color, smooth and well delimited.

The laryngeal fibroma is described as a benign tumor that appears isolated or in patients that suffer of fibromatosis. Due to its rapid growth and extension, this tumor presents an aggressive potential. The most common sites of discovery for this tumor are: the aryepiglottic fold, Reinke's space and the anterior two thirds of the vocal cords.

Laryngeal amyloidosis represents an affliction characterized by the extracellular accumulation of eosinophilic material and of fibrillar proteins in the supraglottic space. It is frequently associated with a systemic disease. The patient presents progressive

dysphonia or shortness of breath. Indirect laryngoscopy reveals a yellow or yellow-grey mass, of waxy consistence and without ulcerations<sup>8</sup>.

The cystic tumors described in the larynx include pathological types such as the epidermal cyst, which is a laryngeal congenital pseudo-tumor from the submucosa. Clinically, the most important symptom is represented by dysphonia. In order to correctly diagnose the disease, an indirect laryngoscopy, associated with fibroscopy and videostroboscopy are required. These investigations reveal a well delimited submucosal structure which is covered by a pale mucosa. This mass determines a decrease in the vocal cord's vibration. The gold standard for diagnosis is the histopathological exam.

The mucous retentional cyst has multiple sites on the vocal cords where it may appear, however its most frequent localizations are on the ventricular bands, the aryepiglottic folds or the epiglottis – these zones are characterized by a high abundance of mucous glands. This type of cyst represents an accumulation of liquid generated by a glandular dilation; this is also observed during the histopathological examination.

The serous pseudo-cyst is a benign tumor originated from the submucosa. Laryngoscopy reveals either a restricted edema on the vocal cord, or an ear shaped formation.

The laryngocele represents a mucosal herniation from the laryngeal ventricle, filled with air. This mass can vary in size from a pseudo-tumor up to giant structures that may induce acute respiratory distress. It is classified in internal, external and mixed. The internal laryngocele causes dysphonia which can sometimes associate shortness of breath, depending on the size of the mass. Fibroscopy reveals a structure in the Morgagni ventricle, on the ventricular bands or on the aryepiglottic fold. The external laryngocele must be distinguished from other tumors or latero-cervical swellings. The laryngocele usually contains liquid which may also become infected, thus causing signs of acute inflammation (laryngopyoceles).

The laryngeal myxoma represents an extremely rare benign tumor originating from the mesenchymal cells. The clinical manifestations, mainly dysphonia and dysphagia, are related to the localization and the size of the mass. The most frequent sites of the tumor are on the vocal cords, the aryepiglottic folds and the epiglottis.

The aberrant goiter represents the enlargement of a supernumerary or ectopic thyroid gland, developed on an embryonic remainder from the thyroglossal duct. Laryngeal endoscopy describes a spherical mass, variable in size, mobile, with a rich blood supply and not painful on palpation. Symptoms may include mild dysphagia, progressive shortness of breath and

eventually drooling with blood drops. The diagnosis is established based on the clinical manifestations, on the radioactive iodine uptake and on scintigraphy.

Benign tumors of the larynx represent pathological entities with a variable incidence which equally affect both genders. These lesions derive from components of the larynx or embryonic remnants. Symptomatology depends on the location and size of the lesions. 80% of the tumors are supraglottic, followed by the glottic and subglottic location<sup>3</sup>.

Positive diagnosis of these tumors is based on symptomatology (persistent hoarseness, shortness of breath, sore throat, pharyngeal paresthesia), followed by clinical examination with videoendoscopic methods, with imaging examination in some cases, and last but not least, the anatomopathological exam which confirms the diagnosis.

Laryngeal papilloma is divided in two types: juvenile and adult-onset papilloma. Laryngeal papilloma is the most frequent benign tumor in children and is determined by the infection of the larynx mucosa with papilloma virus. Lesions are multiple and diffuse, situated on the upper airways, where there is a turbulent airflow and a pronounced dryness of the epithelium, and also in the transition epithelium areas, from the ciliated to the squamous ones. The illness has an extensive and recurrent character, which in severe forms requires a total laryngectomy.

From the 90 subtypes of the virus, the most frequent ones are subtype 6 and 11. Subtype 11 is responsible for the most aggressive form of the disease, with frequent recurrences and extended lesions. Adult papillomatous lesions are unique (horn-like papilloma), rarely associated with viral infection, and present a high malignancy rate due to the association with smoking (a precancerous condition). In these cases, narrow band imaging examination (NBI) allows thorough examination of the lesions in order to increase diagnostic accuracy.

Vocal fold nodules are thickening of the mucosa lining situated on the free edge of the fold. Their appearance is in direct correlation with vocal stress, being frequently encountered on singers, actors, lawyers, teachers, priests etc<sup>5</sup>. The size of the nodules is not proportional with the vocal affliction. Vocal rest can partially alleviate the symptoms, while a high vocal effort can induce long periods of aphonia.

Larynx polyps are the most frequent benign tumors encountered on adult age. Histologically, they are angiofibromas, epithelial tumors with their own conjunctive - vascular axis.

Laryngeal adenoma is a rare tumor which originates from the glandular laryngeal tissue, due to the presence of minor salivary glands of the supraglottic area. Their frequent localization is on the epiglottis.

Differential diagnosis is made with all benign laryngeal lesions, especially with angioma, lipoma, fibroma. According to the literature, malignization may be possible.

Angiomas are benign nonepithelial tumors of vascular endothelium without a vascular -conjunctive axis. It is a rare subglottic pathology which affects especially children. Angiomas are frequently localised on epiglottis, aryepiglottic folds, vocal cords, but also in the same time may affect hypopharynx and base of the tongue. Most of the lesions are unique, but in the literature have been reported also in Rendu-Osler disease or Sturge-Weber disease<sup>3</sup>.

Chondromas are benign cartilaginous tumors which frequently originate from the cricoid cartilage. They present a high rate of recurrence in case of incomplete resection of the tumor, with local extension which may lead to a total laryngectomy.

Laryngeal lipomas are rare supraglottic pathological entities. Dyspnea is the most frequent symptom which may evolve to acute respiratory failure. Differential diagnosis of these lesions is mainly done with internal laryngocele or mucous retention cyst<sup>3</sup>.

Seldom benign tumors with a nervous tissue origin may appear into the larynx. Neurofibroma has a high rate of recurrence, which in 10% of the cases may become malignant, a neurofibrosarcoma<sup>3</sup>. Schwannoma originates from the internal branch of superior laryngeal nerve, it may also affect sensitive and sensory nerves. Histopathological diagnosis is established on three major criteria: the presence of capsule, of Antoni A or B area and positive reaction for S-100 protein. Myoblastoma, described by Abrikossoff for the first time, appears extremely rare into the larynx, exclusively in the posterior area of the vocal folds.

Larynx paraganglioma is a rare, well vascularized tumor that requires a preoperative arteriography. The majority of these tumors are located at the supraglottic level<sup>10</sup>.

Fibromas of the larynx are extremely rare tumors which can appear isolated or in the context of fibromatosis. A careful endoscopic examination is required in order to differentiate them from vocal fold nodules or polyps.

Amyloidosis is a rare larynx affliction that most of the time appears in a general context, but there have been documented cases of primary larynx amyloidosis, without systemic signs of disease. It appears at the supraglottic level, most frequently in the laryngeal vestibule. After histological confirmation, the patient must be investigated for the differential diagnosis between primary systemic amyloidosis and secondary amyloidosis. This disease has a high relapse rate.

The laryngeal epidermoid cyst is a congenital tumor with fluid content, which clinically starts with



dysphonia and can appear in childhood, although it is frequently encountered in adult life. The voice is low-pitched, high-pitched notes being frequently hard to transmit. Its evolution tends to spontaneous drainage, and the remaining lesions can affect the vibrations of the vocal cord<sup>3</sup>. The clinical aspect varies depending on the cyst type (saccular, retention, ductal, vascular, post - traumatic). The epidermoid cyst is located on the upper side of the vocal folds.

The mucous retention cyst doesn't usually communicate with the inner larynx and it's located on the free edge of the vocal folds.

The serous pseudo - cyst is a unilateral benign tumor. Videostroboscopy often shows a supple vocal cord, fact that leads to diagnosis confusions<sup>2</sup>.

Literature data associate laryngocele with vocal effort, some professions like musicians are more likely to develop this kind of lesion. Differential diagnosis is often difficult, because of its high variability in dimensions. Internal laryngocele can be found in the inner larynx and the external type can exceed the thyroid cartilage boundary, traverses the thyrohyoid membrane and is exteriorized in the laterocervical region. Valsalva maneuver determines an expansion of the tumor because of the air that reaches inside it.

Larynx myxoma can achieve great size that can determine airway obstruction, with the necessity of performing a tracheostomy<sup>11</sup>.

Aberrant goiter tissue is often found on the base of the tongue. For a positive diagnosis, a thyroid scintigraphy with I<sup>131</sup> is necessary, that identifies the ectopic tissue and helps to localize it.

## CONCLUSIONS

Laryngeal benign tumors are pathological entities that display a high variability in terms of

incidence and histologic origin, with nonspecific clinical appearance. The exact diagnosis will be established by histological and immunohistochemical examination. An efficient and optimal therapeutic attitude depends on the accuracy of these investigations.

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