Surgery for Benign Tumors of the Adult Larynx

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Core Messages

- Benign neoplasms of the larynx are uncommon, with the exception of papillomas, which comprise up to 95% of this group.
- Symptoms associated with these benign tumors reflect site and size; in general, dysphonia, dyspnea, and dysphagia are the most common patient complaints and a cause should be thoroughly sought.
- The diagnosis of a benign laryngeal neoplasm, although suspected by the duration of the history and the physical examination, must be confirmed by biopsy or at least investigation when a vascular neoplasm is suspected (e.g., hemangioma or paraganglioma).
- Certain tumors have a predilection for anatomical sites in the larynx. The supraglottis is the most common site (80%), followed by the glottis and subglottis. This information may hinder the accuracy of the diagnosis if one relies on the clinical examination alone.
- Once diagnosed, most benign neoplasms can be treated by surgical excision. The surgical approach and excision depend on the tumor size and location; but in general, preservation of laryngeal function is the primary aim of treatment in the form of complete excision with tumor-free margins.
- Certain neoplasms—papillomas, oncocytic tumors, pleomorphic adenoma, lymphangiomas, neurofibromas, fibromatosis, paragangliomas, rhabdomyomas—have a tendency to recur, be it months or even years, following incomplete excision.
- Differentiation of benign from malignant tumors is vital. Paragangliomas, neurofibromas, and chondromas, among others, have malignant variants, with certain granular cell tumors, hemangiopericytomas, and others having histological features that mimic those of malignant disease. Reliance on expert histopathologists is crucial for accurate, appropriate treatment.
- With improvements in imaging, histopathology, and surgical techniques—endoscopy, microscopic magnification, application of lasers—there has been marked improvement in the accuracy of diagnosis and the ability to perform precision excision surgery for benign tumors. This means more preservation and restoration of laryngeal function than was previously possible.

7.1 Introduction

7.1.1 Background

The delicate balance between surgery and preservation of organ function can have no greater illustration than within the larynx. Treatment of any laryngeal disorder requires a detailed knowledge of both diagnostic

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and therapeutic surgical interventions and their impact on vocal and laryngeal function. Whereas the objectives of surgery for malignant tumors permit a more pyrrhic approach, surgery for benign laryngeal tumors demands particular consideration and application. Furthermore, a thorough appreciation of the pathological processes at work and their prognostic significance aid surgeons in making the best possible treatment choices for their patients.

7.1.2 General Principles

The presence of a mass lesion in the larynx can provoke numerous acute, chronic, progressive, or even life-threatening symptoms. When assessing the patient with a potential laryngeal tumor, a thorough history should be taken with particular emphasis on the age of the patient, the temporal course of the symptom complex, the presence of infection, any previous surgery or trauma, and the presence or absence of respiratory, vocal, or swallowing symptoms—all of which give clues as to the nature and extent of any tumor. Although the experienced laryngologist may be able to make an accurate clinical diagnosis using a flexible nasendoscope in the outpatient clinic, evidence suggests that the accuracy of diagnosis based on visual examination alone is subject to some variation [10].

The initial decision to operate depends on detailed visual inspection of the lesion, histological diagnosis, and a need to establish that the tumor is not malignant. Also, a contemporary meticulous endoscopic examination of the entire upper aerodigestive tract is required to assess the size, position, consistency, and extent of any tumor, in addition to excluding any concurrent aerodigestive tract pathology. Furthermore, information relating to endoscopic and surgical access and the potential for resection should be carefully considered when planning future definitive surgical management. Indications for surgery beyond this first therapeutic step include failure of conservative measures, symptomatic relief, maintenance of organ function, and concern about any potential for malignant transformation. Ultimately, the method by which resection is done is dependent on both tumor and patient factors, the experience of the operating surgeon, and the facilities available to them.

7.1.3 Classification

The definition of noncancerous or benign tumors of the larynx requires some elaboration. In 1938, New and Erich [51] published the Mayo Clinic experience of 722 patients presenting with benign laryngeal pathology. The authors proposed that as true proliferative neoplasms were often clinically indistinguishable from nonproliferative inflammatory or hyperplastic growths the term *benign tumor* should be used to encompass all abnormal growths of tissue in the larynx that lacked malignant or metastatic properties. In 1951, a similar analysis of 1197 patients with benign laryngeal growths by Holinger and Johnstone [30] assented to the New and Erich recommendation. Since then, some authors have revised the concept, classifying vocal fold nodules, laryngeal polyps, cysts, and nonspecific granulomas to be mucosal reactive inflammatory disorders and therefore nonneoplastic in nature [5].

Notwithstanding these various viewpoints, the principles of management remain analogous. A nomenclature based on the authoritative surgical head and neck pathological tomes [5, 44] is shown in Table 7.1. True benign neoplastic tumors of the larynx are rare (Table 7.2). New and Erich [51] reported around 210 such tumors in a series of 722 patients presenting over a 30-year period. Among them, 194 of the 210 (92%) were squamous papillomas. Holinger and Johnstone [31] reported a similar series collected over 15 years. They reported 125 true benign tumors, of which 115 (92%) were papillomas. In a series from Pittsburgh, Barnes [5] reported 404 true benign neoplasms over a period of 38 years. Among these patients, 326 (81%) had papillomas; the remaining 78 (19%) were classified as nonpapilloma lesions. A combined European series from the university departments in Marburg and Giessen, Germany, reported [23] 181 true benign neoplasms in a series of 2223 benign tumors or tumor-like lesions. Of these tumors, only 32 were not papilloma-related. Contemporary series concur with these early findings and show that the papilloma accounts for up to 95% of all nonmalignant laryngeal tumors [50] (Table 7.2). Thus, otolaryngologists may expect to see only a handful of cases during their careers.

The present chapter concentrates on surgery for those lesions considered “true” benign proliferative neoplastic tumors. We reserve the management of

Table 7.1. Pathological classification of benign laryngeal tumors

Epithelial
Squamous epithelium
Recurrent respiratory papillomatosis
Keratinized papilloma
Glandular
Pleomorphic adenoma
Oncocytic tumor
Nonepithelial
Vascular
Hemangioma
Lymphangioma
Cartilage and bone
Chondroma
Giant cell tumor
Muscle
Leiomyoma
Rhabdomyoma
Angiomyoma
Epithelioid leiomyoma
Adipose
Lipoma
Neural
Neurilemoma
Neurofibroma
Paraganglioma
Granular cell
Pseudotumors
Fibroma
Inflammatory fibroblastic
Amyloid
Laryngeal cysts

reactive mucosal and inflammatory lesions for another discussion.

7.2 P apillomas

7.2.1 General Considerations

Squamous papillomas are the most common benign tumors of the larynx. Barnes (2001) [5] classified papillomas into two histological types: keratinized and nonkeratinized. Keratinized papillomas (papillary keratosis) occur mainly in adults and are mostly solitary lesions that arise from the true vocal cord. Most keratinized papillomas are not related to viral infection but are associated with smoking; they can be associated with malignant transformation. Keratinized papillomas variably recur following simple excision [5]. Recurrent respiratory papillomatosis (RRP), or nonkeratinized papilloma, is the most frequently occurring benign laryngeal neoplasm. The estimated incidence is around 4 per 100,000 population in children and 1–2 per 100,000 population in adults [13, 56]. A disease of viral etiology, RRP is both a neoplastic and an infectious phenomenon caused by the human papilloma viruses (HPV). More than 90 subtypes of HPV are recognized, with HPV-6 and HPV-11 most commonly found in laryngeal papilloma [76]. RRP occurs in response to mucosal infection with HPV and can develop on any mucosal surface of the upper aerodigestive tract. RRP has a tendency to form at anatomical sites of junctions between squamous and ciliated epithelium: papillomas occur most often at the nasal valve, the nasopharyngeal surface of the soft palate, the laryngeal surface of the epiglottis, the upper and lower margins of the ventricle, the undersurface of the vocal folds, the carina, and at bronchial spurs. The most frequently affected site at diagnosis in both the pediatric and adult populations is the larynx (Fig. 7.1).

The incidence of RRP is bimodal, giving rise to two distinct forms: juvenile onset and adult onset [14]. The juvenile onset variant RRP (JO-RRP) is more aggressive than the adult form. Most investigators consider RRP to be of adult onset if the patient is older than 16–20 years of age at diagnosis. Adult-onset RRP is diagnosed most frequently between the ages of 20 and 40 years and shows a slight male preponderance [13].

In RRP, HPV-11 subtypes have been shown to have a more aggressive clinical course, with higher rates of recurrence, poorer response to adjuvant therapy, greater respiratory spread, and increased need for tracheostomy [21]. Some authors have recommended that all patients with RRP should undergo HPV typing early in the course of the disease. Identification of those patients with high-risk subtypes would theoretically allow modification of treatment regimens, such as by early intervention with adjuvant therapy. The incidence of carcinoma developing in patients with RRP is reported at 1–7% [5, 57]. Laryngeal cancer complicating RRP has an increased association with HPV-11, HPV-16, and HPV-18 infection, previous exposure to radiation, and the JO-RRP variant [5, 22, 57]. As patients with RRP may also be heavy smokers and drinkers, larger studies are required to clarify any causal or synergistic relation that may exist between HPV (and/or its subtypes), RRP, and carcinogenesis. (Fig. 7.2)

Table 7.2. Select series of benign laryngeal tumors

	New	Holinger	Barnes	Narozny	Glanz
Series duration (years)	30	15	38	45	12[b]
Total no. of true proliferative neoplastic tumors	210	125	404	291	171
Squamous papillomas[a]					
Total	194 (92%)	115 (92%)	326 (81%)	277 (95%)	149 (82%)
Nonsquamous papillomas					
Adenoma	1	0	0	1	1
Chondroma/osteochondroma	7	2	3	2	5
Fibroma	6	0	0	0	0
Fibromatosis	0	0	1	0	0
Fibrous histiocytoma	0	0	2	1	3
Granular cell	0	0	12	2	2
Hemangioma	Unknown[c]	4	9	6	8
Lipoma	1	0	3	0	5
Lymphangioma	0	1	2	0	1
Myxoma	Unknown[c]	0	0	0	0
Neurilemoma	0	0	2	1	1
Neurofibroma	1	1	3	1	0
Nodular fasciitis	0	0	1	0	0
Oncocytic	0	0	35	0	0
Other	0	2	0	0	3
Paraganglioma	0	0	2	0	3
Adenoma	0	0	1	0	0
Rhabdomyoma	0	0	2	0	0
Total	16 (8%)[c]	10 (8%)	78 (19%)	14 (5%)	32 (18%)

[a]Includes adult and juvenile variants
[b]Two 6-year series combined
[c]Authors unsure of precise nature of many angiomas and myxomas with most estimated to be of inflammatory etiology and only "a few" true neoplasms

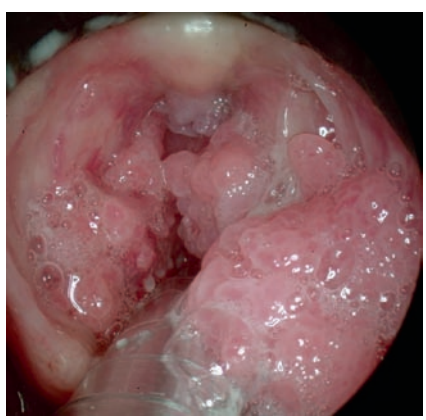

Fig. 7.1. Recurrent respiratory papillomatosis (RRP). Endoscopic view

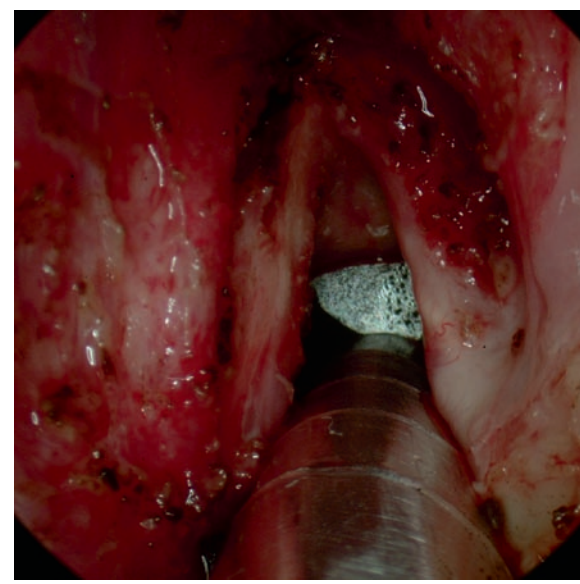

Fig. 7.2. Recurrent respiratory papillomatosis (RRP). After CO_2 laser AcuBlade ablation

7.2.2 Indications

The main indications for surgery in patients with RRP are the need for histological diagnosis, maintenance of an adequate airway, and preservation of laryngeal and vocal function. As RRP represents an as yet undefined alteration of mucosal immunosurveillance rather than a simple mechanical change, surgery for the disease is rarely curative even after en bloc resection of the papillomatous epithelium. Latent HPV DNA has been shown to be present in biopsy specimens from uninvolved sites and from patients in apparent remission. As the epithelium regenerates after surgery, reinfection occurs from virus present in this "normal"-appearing mucosa [58]. The philosophy of surgery for RRP must be altered accordingly. In this situation, the tenet of "less is more" applies. Removal of disease most commonly occurs under general anesthesia. Some patients with mild disease require only a few treatments. Patients with more aggressive variants can require monthly or bimonthly surgery to promote disease regression. This is one reason why office-based procedures are gaining popularity (see below).

7.2.3 Specific Assessment

The most common presenting symptom of RRP in adults is some degree of hoarseness or dysphonia and sometimes shortness of breath. These voice changes may be subtle and can persist for many years. Occasionally, adult-onset RRP behaves like the more aggressive juvenile variant. Here, the patient may develop progressive dyspnea, stridor, and even acute life-threatening airway compromise. Preoperatively, it is useful to evaluate the location and morphology of the papilloma using a flexible nasendoscope. Macroscopically, papillomas are pink or white, sessile or exophytic, pedunculated or broad-based. Occasionally, the papilloma develops across a wide field, appearing like a carpet or velvety sheet of disease, requiring high levels of magnification to localizes it accurately. As the disease can affect different anatomical sites in the larynx, it is important for the surgeon to be comfortable with several surgical methods and instruments. Consideration of these characteristics can guide the surgeon to select the most effective resection technique.

7.2.4 Surgical Techniques

For treating RRP, the menu of surgical options include microsurgical cold steel, carbon dioxide (CO_2) laser, microdébridement, and office-based angiolytic laser treatment. As new techniques have been developed, some investigators have preferred one method over another [20]. The approaches for surgical removal of RRP remain controversial. It should be remembered that no surgical method has been shown to eradicate RRP; therefore, it remains a chronic disease where surgical techniques and instrumentation should be selected to enable the surgeon to achieve the goals of surgery as described above.

7.2.5 CO_2 Laser

The principals of CO_2 laser ablation are relatively simple. At a wavelength of 10,600 nm, light is converted to thermal energy, which is absorbed by water in the target tissues. This causes tissue destruction by vaporization at the molecular level. Two modes—pulsed and continuous—are currently in common use. The pulsed mode produces the fastest vaporization, the least collateral thermal injury, and the least char. Pulsed mode at low power (up to 5 W) allows control over the incision, prevents adjacent thermal damage to the anterior commissure, and avoids a hole of unintended depth (while pausing). Bleeding can be a problem with the pulsed mode, whereas the continuous mode results in more coagulation but with more risk of collateral thermal injury. Manipulation of the laser spot size and "mode" allows the operator to switch between vaporization of large areas of bulky disease or more precise targeted removal of smaller areas.

The CO_2 laser operative techniques are described in detail elsewhere. However, in brief, this is our approach. The operating team consists of a lead scrub nurse, a laser nurse, and a circulating nurse. The laser nurse is free to manage the laser, allowing the other members of the team to concentrate on their duties. All personnel wear protective goggles and approved laser filtration masks with spare goggles and appropriate warning signs placed outside the operating room. The room is set up with the suspension microlaryngoscope system of choice; a selection of laryngoscopes, ventilating bronchoscopes; and Hopkins Rod telescopes; and a set of suction and

microlaryngeal instruments. An operating microscope is fitted with a 400-mm lens and a CO_2 laser micromanipulator. A video-endoscope "stack" equipped with a monitor, light source, and digital recording equipment is also used. The anesthesia technique during laser surgery reflects personal preference, experience, and institutional protocols. Nonintubation methods are popular and include spontaneous breathing, apneic, and jet ventilation techniques. The advantages of these methods include no flammable material in the airway so the risk of fire is minimized and there is excellent visibility of the surgical field. Intubation techniques utilize "laser safe," or "armored," endotracheal tubes, and care must be taken to use them in accordance with the manufacturers' recommendations.

Precise operation of the laser depends on the location and morphology of the lesion or lesions. Generally, a defocused spot in continuous mode is utilized for bulky lesions, and a narrow focus spot size in pulsed mode is reserved for areas where minimal damage to laryngeal structures is desired. Andrus (2005) [2] described a "laser brush" technique for sessile papillomatous growth. With this method, the laser is set to the lowest power setting (2–3 W) that allows adequate vaporization of tissue. The time exposure is set at 1 second and the spot size diameter at 0.3 mm. The laser is then applied to the broad surface of the papillomas in brush strokes in an anterior-to-posterior direction. This causes superficial vaporization and carbonization of the surface of the lesion. The char is removed with a saline-soaked neurosurgical pad ("the brush") and microsuction. The depth of removal can easily be assessed at high magnification and the laser used in repeated brush strokes until the uninvolved submucosal layer is identified (Fig. 7.3).

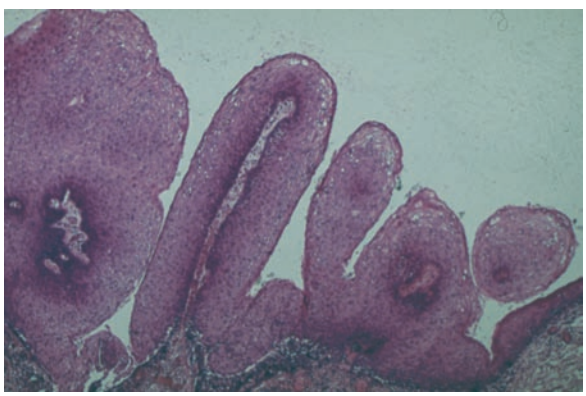

Fig. 7.3. Recurrent respiratory papillomatosis. Microscopic view (H.E)

7.2.6 Angiolytic Laser Treatment

The philosophy of angiolytic laser treatment for RRP appears a sound one. In theory, laser energy between 500 and 600 nm wavelengths is selectively absorbed by intravascular oxyhemoglobin, resulting in coagulation of target tissue vasculature. In contrast, CO_2 laser energy at 10,600 nm is absorbed mainly by water, the primary constituent of most human tissue. Control over CO_2 laser selectivity is therefore limited, and collateral damage to normal tissue is predictable. In 1998, investigators demonstrated application of the 585-nm pulsed dye laser (PDL) to RRP in the human larynx. Early results showed that, compared to the CO_2 laser, PDL was capable of comparable levels of disease regression and reduced risk of normal tissue damage [20]. A further advantage of PDL is that it can be deployed in the office setting under local anesthesia [12, 20].

Treatment with PDL may be associated with some complications, including perivascular extravasation, which appears as a characteristic "purpura" in the surrounding tissues at surgery. Bleeding occurs when blood in the vessel lumen is heated too rapidly, leading to vessel wall rupture before coagulation has occurred. This can be avoided by balancing the relatively short pulse width of the PDL (0.5 ms), the energy settings for that pulse, and delivery of the amount of energy required for coagulation to a moving target (varying fiber-to-tissue distance.) The loss of operative visualization, the patient coughing, and/or the inevitably absorption of laser energy by blood in the surrounding area rather than the target tissues can limit use of the PDL [20].

Issues surrounding the size of the PDL fiber (0.6 mm) and coupling it to the working channel of existing fibreoptic equipment has led to interest in the potassium-titanyl-phosphate (KTP) laser as an alternative angiolytic application. The KTP laser wavelength of 532 nm is strongly absorbed by oxyhemoglobin, and its small fiber diameter of 0.3–0.4 mm allows easier use with existing flexible laryngoscopes. Furthermore, in theory adjusting the pulse width to 15 ms allows slower, more uniform coagulation with less extravasation and collateral photothermal injury [81]. One weakness of both PDL and KTP angiolytic laser therapy is that they are not as effective for bulky disease as conventional surgery.

It may be that utilizing cold steel, microdébridement, or CO_2 laser as an initial treatment strategy with angiolytic laser therapy reserved for maintenance or

follow-up surgery will evolve. Some predict that outpatient-based angiolytic laser therapy will supplant CO_2 laser ablation as the primary mode of follow-up surgical management for RRP [2, 81].

7.2.7 Microdébrider

Adaptation of the powered microdébrider system for laryngeal use in RRP was first reported by Myer in 1999 [47]. Equipped with suction, angled oscillating blades, and irrigation, the microdébrider system can be deployed in the larynx under suspension laryngoscopy or in conjunction with a handheld Hopkins rod. Refinements and proliferation of instrument designs have led to the growth in the popularity of this system, and supporters claim several safety advantages over the CO_2 laser. They include the absence of a laser plume, no risk of ocular or other laser injury to the patient or personnel, and no risk of airway fire. Furthermore, use of the microdébrider system is less intensive in terms of equipment charges and operating room staff. Some investigators report a significant reduction in operating times and increased cost-effectiveness compared to similar CO_2 laser procedures. A survey of members of the American Society of Pediatric Otolaryngology showed that use of the microdébrider has overtaken the CO_2 laser as the method of choice for surgical removal of papillomas in the pediatric population [65]. However, those who advocate preservation of as much of the remaining (voice-producing) superficial lamina propria as possible suggest that the technique is insufficiently controlled, especially for patients desiring a career of professional voice use.

7.3 Adjuvant Therapy

7.3.1 General Considerations

Some progress is being made toward developing effective medical treatment for RRP, and these authors hope that the the surgical treatments discussed above will one day be outdated. Current antiviral adjuvant treatments in limited use for RRP include cidofovir, interferon-α, and indole-3-carbinol. Novel agents undergoing Phase III trials include fusion proteins (heat-shock-protein E7,) and cyclooxygenase-2 inhibitors (celecoxib.) Furthermore, prophylactic immunization against HPV infection, as licensed for cervical HPV infection in young women, is now possible, although large populations would need to be treated to prevent one case. There are currently no formal guidelines, and no substantial randomized controlled trials of adjuvant therapy for RRP. The decision to offer adjuvant therapy therefore must be individualized and based on the frequency of surgical interventions, the morbidity of frequent surgeries, and the recurrence pattern of the papillomas balanced against the possible risks and side effects of these agents (e.g., the possible mutagenic effects of cidofovir). Examination of the available retrospective literature suggests that patients requiring four or more surgical interventions per year for 2 years, suffering from distal, multisite spread of the disease, and/or rapid regrowth with airway compromise might be candidates for adjuvant treatment [14, 65]. Furthermore, as the clinical evidence defining the precise role for these adjuvant therapies is limited, informed consent and consideration of enrollment in clinical trials are important.

7.3.2 Cidofovir

The use of the intralesional antiviral agent cidofovir {1-[(*S*)-3-hydroxy-2-(phosphonomethoxy)propyl] cytosine dihydrate} (HPMPC) in RRP was first described in 1995 [72]. Since then numerous studies have reported favorable results in terms of disease regression and remission following direct intralesional injection in adults [15, 54]. Interpretation of these and other data is complicated by the wide variation in the total dose given (2–57 mg), the frequency (2–8 weeks) and duration of treatments (months to years), and the concurrent use of surgical and other adjuvant treatments [67]. In addition, the heterogeneity in case series between adult and juvenile populations further confounds the interpretation of outcomes.

The precise dose, frequency of administration, and duration of treatment for cidofovir in adults with RRP is unclear. Systemic toxicity for intralesional cidofovir seems low [68]. Some studies have reported the use of cidofovir in the adult population using concentrations of 2.5–6.5 mg/ml with volumes of up to 6–8 ml per therapeutic session, administered every 2–4 weeks for up to 19 months. Others have utilized higher concentrations (37.5 mg/ml) delivered in smaller treatment volumes (up to 57 mg per therapeutic session) via a

percutaneous route [11]. The use of cidofovir therefore remains controversial. We recommend using intralesional cidofovir in moderate to severe disease where there is a need for frequent surgery and deteriorating vocal and airway function. Furthermore, informed consent should be obtained after detailing the potential side effects including nephrotoxicity and carcinogenesis risks. Concerns over long-term efficacy and potential side effects of malignant transformation mandate adequately powered randomized, controlled trials.

7.3.3 Interferon-α

The interferons are a group of natural proteins produced by the body in response to infection. Interferons may be classified as alpha, beta, or gamma and are named after their ability to interfere with viral replication. These substances have been synthesized for clinical use using recombinant DNA techniques. In therapeutic doses, interferon can produce considerable side effects, including flu-like symptoms such as fatigue, headache, and general aches as well as, less regularly, hypothyroidism, arthritis, thrombocytopenia, and psychiatric disturbances. In 1981, Haglund [26] described the use of human leukocyte interferon in a small cohort of patients with RRP. Since then, various studies have demonstrated the usefulness of interferon-α in severe RRP requiring frequent surgical interventions [22, 28, 38]. The long-term effectiveness of interferon-α is still controversial [2, 22, 38]. Combined with its side effect profile and the development of newer adjuvant strategies, the use of interferon-α in RRP seems to be declining [65], and we suggest that it be reserved as a third-line treatment for patients with airway obstruction.

7.3.4 Specific Recommendations According to the Technique

It is important to remember that RRP is not typically cured by surgical removal of disease, and the infectious nature of RRP eventually manifests as a recurrence. An aggressive surgical strategy therefore does not lead to reduced recurrence or a chance of cure. It should also be understood that RRP is limited to the surface epithelium. The principles of surgery, irrespective of the technique chosen, should be tailored to precise, careful removal of the disease taking into consideration the preservation of underlying structures and vocal function. This is particularly important in relation to the glottis and subglottis, where overly aggressive ablation can result in severe scarring and dysfunction. Preservation of even small areas of mucosa with intact superficial lamina propria may make a huge difference to voice outcomes Extreme care should be taken in the areas of the anterior and posterior commissure. Papillomas should not be removed from both sides of the anterior or posterior commissure simultaneously as it can lead to web formation. An anterior commissure spatula or retractor should be used to protect one side of the anterior commissure while laser ablation or laser excision is performed on the other side.

7.3.5 Recommendations for Follow-Up (Postoperative Care)

We encourage patients with stable disease requiring fewer than three or four procedures per year to self-refer as often as they feel it is necessary. For new patients, frequent office visits are employed to develop trust and a good working relationship. However, the development of more reliable, fast, low-morbidity office-based treatments may alter this stratagem.

7.4 Hemangioma

Laryngeal hemangiomas are rare but important as they may present with significant airway obstructive symptoms. Ferguson [18] classified hemangiomas into two groups: pediatric (10%) and adult (90%) types. The pediatric type is typically subglottic (Fig. 7.4). The pathogenesis of hemangiomas remains controversial as to whether they represent a true neoplasm or a congenital abnormality. Their behavior is sometimes aggressive, in which case it should be considered a malignant neoplastic lesion. When such lesions present in the adult, they usually arise on or above the vocal cords, and patients present with vague, often extended histories of hoarseness and occasional dysphagia. These tumors are seen more frequently in men (60–70%), and most are cavernous-type hemangiomas (the others being capillary type). The tumors are mostly rounded, projecting or pedunculated, purplish growths

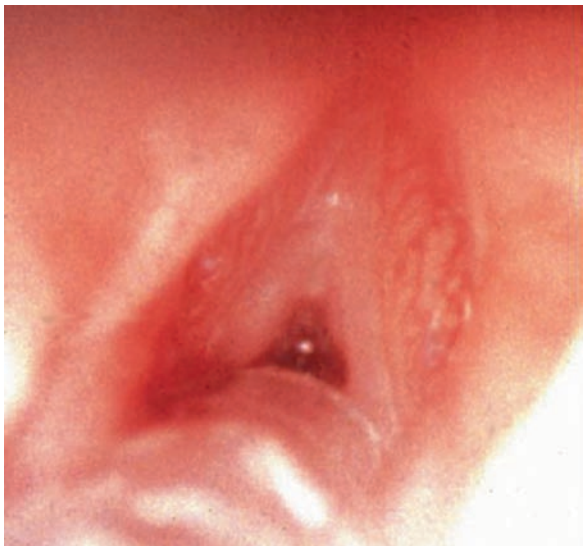

Fig. 7.4. Pediatric subglottic hemangioma (horseshoe shape)

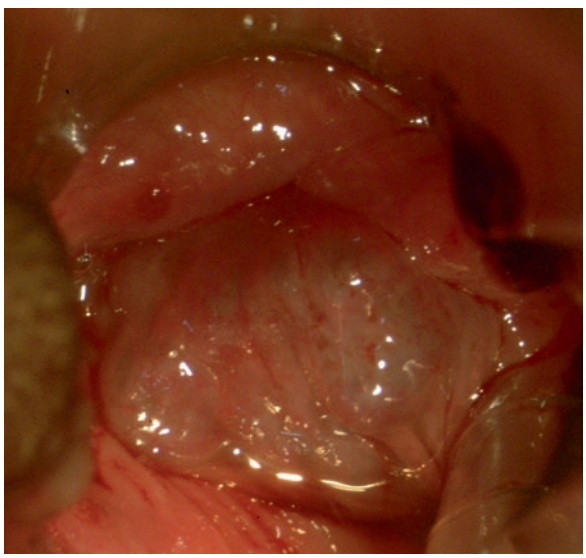

Fig. 7.5. Hemangioma of the left arytenoid of an adult patient

arising on or above the vocal cords. Occasionally, they are larger sessile tumors that extend submucosally into the laryngopharynx (Fig. 7.5) [36]. As a rule, the only symptom is hoarseness, and they rarely progress to the point of causing respiratory narrowing or obstruction. Although most angiomas are benign growths, some are multicentric and the term "hemangiomatosis" is applied; these lesions may be part of a variety of clinical syndromes such as Rendu-Weber-Osler and the Sturge-Weber dyscrasia.

7.4.1 Management

Surgery is the treatment of choice, but the potential for severe hemorrhage during biopsy or excision is well documented [18]. Since the introduction of laser therapy for vascular lesions, the management of laryngeal hemangiomas has proven useful. The use of photocoagulation with Nd:YAG laser has offered the clinician an effective alternative therapy that is minimally invasive and has few complications [80]. Success also has been reported with the use of CO_2 laser excision. Occasionally, use of the laser requires staging and time spacing of the surgical procedure to allow complete resolution of the postoperative laryngeal tissue inflammation and edema. Some patients require a temporary tracheostomy during the course of these laser procedures [41].

7.5 Hemangiopericytoma

Hemangiopericytomas are rare but are highlighted because they can present diagnostic and histological dilemmas (Fig. 7.6) [7]. These lesions present as a supraglottic cyst-like mass that usually has a vascular-type appearance. The mass is firm, solid, pedunculated

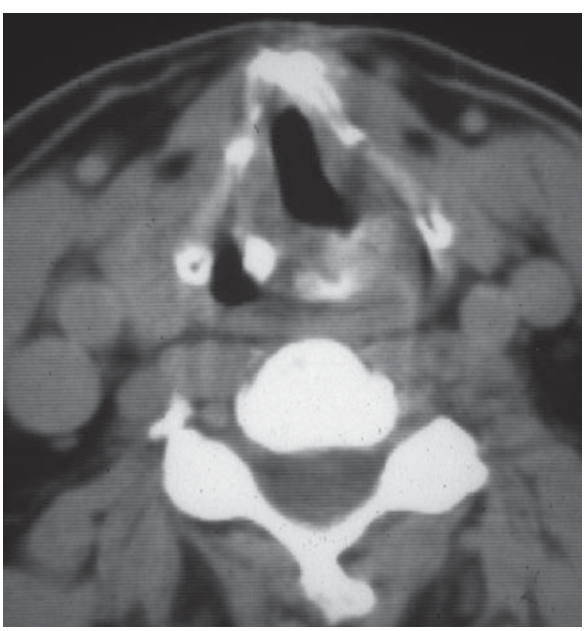

Fig. 7.6. Hemangiopericytoma developed from the subglottic area. Computed tomography (CT) of the right side of the cricoid cartilage

or nodular, usually well circumscribed, in a submucosal location, and is up to 4 cm in greatest diameter. The surface is covered by intact epithelium with dilated vessels. Histologically, the tumor has few mitoses. Occasional increased cellularity, pleomorphism, and mitotic activity are associated with recurrences or metastases in other anatomical locations [49]. The differential diagnosis includes hemangioma, angiosarcoma, glomus tumor, fibrous histiocytoma, leiomyoma, synovial sarcoma, malignant melanoma, leiomyosarcoma, spindle squamous cell carcinoma, and mesenchymal chondrosarcoma [49].

7.5.1 Management

Surgical treatment is recommended and may necessitate total laryngectomy (Fig. 7.7), although lesser surgical procedures have been described. Sadly, long-term follow-up of such cases is lacking to support a laryngeal conservation surgical approach in the light of difficulties with the histopathological diagnosis.

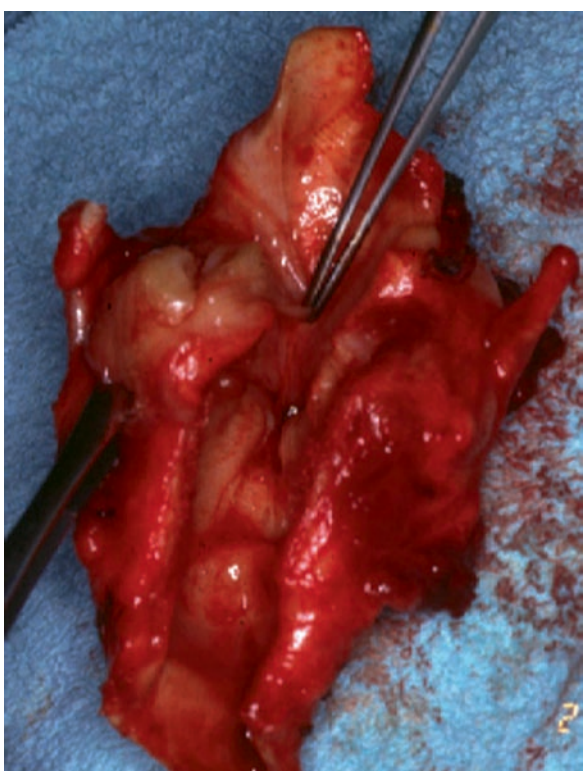

Fig. 7.7. Hemangiopericytoma. Surgical specimen after total laryngectomy

7.6 Leiomyoma

An extremely rare neoplasm, leiomyoma usually occurs in the supraglottic larynx, with the ventricle and false cord most often involved, although leiomyomas of the subglottis and trachea have been described. These tumors arise from smooth muscle and are peculiar in that there is little smooth muscle in the larynx, compared to other parts of the head and neck. The tumors are usually sessile, bulging, or polypoidal red-brown masses that are up to 5 cm in maximum diameter. These masses are usually covered by an intact smooth surface epithelium, with a conspicuous vascular arborizing pattern, although ulceration is noted in larger lesions.

Microscopically, leimyomas are distinctly encapsulated masses located in the submucosa and are composed of spindle cells arranged in fascicles, whorls, and intersecting bundles. Three types of leiomyoma are recognized: the "common" leiomyoma, the vascular leiomyoma (angiomyoma), and the epithelioid (leiomyoblastoma). All three have been identified in the larynx.

The differential diagnosis includes benign peripheral nerve sheath tumors, neurilemomas and neurofibromas, nodular fasciitis, fibromas, and leiomyosarcoma. However, any of the spindle cell tumors (inflammatory myofibroblastic tumor, contact ulcer, fibrosarcoma, spindle cell squamous cell carcinoma, synovial sarcoma) should also be considered.

7.6.1 Management

Surgical excision with clear margins after confirmation of the diagnosis is curative. Because of the vascularity of the angiomas, there is a high risk of significant bleeding, with the possibility of recurrence as a result [1].

7.7 Rhabdomyoma

Rhabdomyomas in the larynx arise from striated muscle and are divided into two subtypes based on their histological features, not on the patient's age at presentation: adult type and fetal cellular type [3]. The current definition of rhabdomyoma is a benign neoplasm of striated muscle tissue, consisting usually of polygonal, frequently vacuolated (glycogen-containing) cells

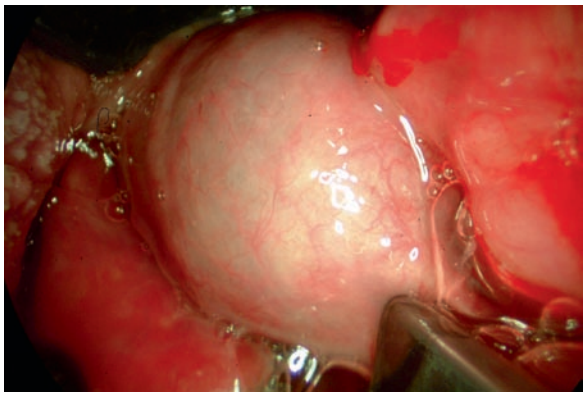

Fig. 7.8. Rhabdomyoma in the aryepiglottic fold

with a fine granular, deeply acidophilic cytoplasm resembling myofibrils cut in cross section [33].

Involvement of the larynx is uncommon [39]. Adult rhabdomyomas occur more frequently in men than women (4:1), with reported ages ranging from 16 to 76 years (mean 52 years). The adult type presents as a single lobulated, polypoidal or pedunculated, nonencapsulated, tan-yellow to deep gray-red-brown mass. Occasionally, these lesions are multifocal, with lesions in more than two locations in the head and neck, including the larynx [40]. They may measure up to 7.5 cm in greatest dimension, but most are 1–3 cm. The lesions have been most frequently located to the supraglottis or vocal cord (Fig. 7.8) [37]. The fetal cellular type of rhabdomyoma has a similar presentation and is usually found in preadolescent patients, although it may affect the head and neck region in elderly men [9]. There is also a fetal myxoid type that is found in the head and neck area of children, especially in the postauricular region, although it has also been reported in the adult larynx [33].

The benign differential diagnosis for the adult type of tumor includes granular cell tumor, oncocytoma, paraganglioma, hibernoma, and alveolar soft-part sarcoma. They are characterized by the presence of a sarcolemma sheath, rod-like cytoplasmic bodies, and cross striations.

7.7.1 Management

Complete surgical excision is curative. Although local recurrences have been reported in more than 33% of cases treated in the head and neck region, which usually result from incomplete resection, it appears not to be associated with rhabdomyomas located in the larynx [31]. Recurrences may present months to years after the initial resection. To date, there has been no documented case of malignant degeneration of the adult-form rhabdomyoma.

7.8 Lipoma

Benign lipomas are commonly encountered in a wide variety of locations throughout the body. It is estimated that 13% of lipomas occur in the head and neck. Laryngeal lipomas are rare, with fewer than 100 cases reported. When present, they are most frequently located in the aryepiglottic fold (Jungehulsing et al. 2005). They are mostly found in adults and primarily affect men, with fewer than 90 cases reported in the literature [75].

In general, these lesions present like cystic lesions: encapsulated, smooth, and usually pedunculated (Fig. 7.9 and 7.10). Symptoms are few and uncharacteristic, making accurate diagnosis difficult. Clinically, they can be confused with other benign lesions, such as retention cysts or laryngoceles [34]. There has been no

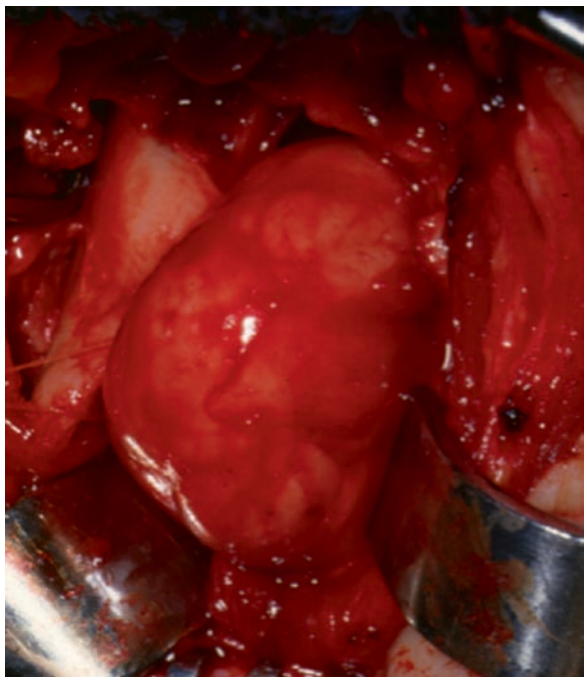

Fig. 7.9. Lipoma. Surgical view during the open neck approach after the laryngeal opening

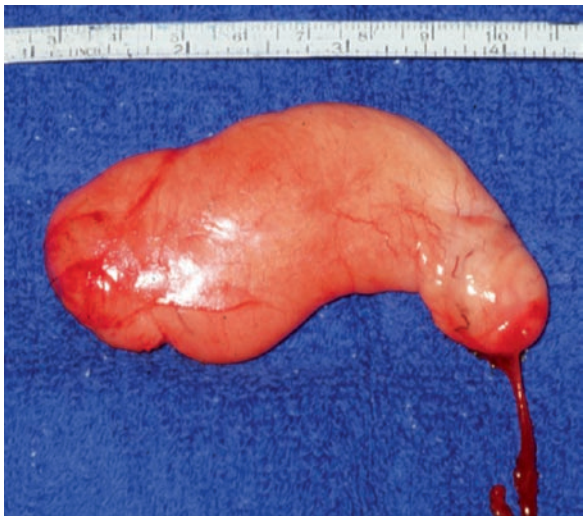

Fig. 7.10. Lipoma. Surgical specimen

report of malignant transformation of a solitary lipoma, although malignant change in multiple lipomas of the larynx and the pharynx has been described [27, 35].

7.8.1 Management

Transoral resection of the lipoma is relatively simple and effective with the use of CO_2 laser. The aim of treatment is always a conservative surgical excision, with preservation of laryngeal function the surgeon's major intent [27]. Although described, recurrence is rare.

7.9 Neurofibromas and Neurilemoma or Benign Schwannomas

Benign neurological lesions are uncommon laryngeal tumors. There are two classes of benign neurogenic tumors of the larynx: schwannomas and neurofibromas, with schwannomas being more frequent. Since the first reported case of laryngeal schwannoma in 1925, more than 130 laryngeal tumors of neural origin had been reported up to 1993 [6], but it is difficult to distinguish the exact number of neurilemomas and neurofibromas.

Most schwannomas present in the parapharyngeal space, with the head and neck accounting for 25–45% identified clinically. The larynx remains a rare site. These tumors in the larynx may present at any age, with a slight female preponderance. Almost all benign neurogenic tumors of the larynx arise in the supraglottis, although the true vocal cord may be involved, with fewer than 10 cases reported [70].

They are more likely to affect sensory nerves than motor nerves and differ from neurofibromas in that the latter are not encapsulated, do not cause symptoms, and may be associated with neurofibromatosis type II (von Recklinghausen's disease) [52]. Neurilemomas affect both sexes equally, and they occur most often during the fifth to sixth decades of life. Neurilemomas typically affect nerve sheaths but not usually the nerve fibers. Neurofibromas may be single or multiple; multiple lesions characterize neurofibromatosis type I [70].

It is important to distinguish between neurofibromas and schwannomas. The recurrence rate is greater for neurofibromas, and malignant transformation from neurofibroma to malignant neurosarcoma occurs in approximately 10% of cases. In contrast, malignant degeneration of schwannomas is extremely rare. Computed tomography (CT) and magnetic resonance imaging (MRI) can help with the diagnosis, revealing not only the extent but the degree of the lipomatous element as well. Compared with CT, MRI offers superior soft tissue definition and better visualization of the laryngeal musculature [69].

The characteristic finding is a round submucosal bulge arising from the false cord and/or aryepiglottic fold, obstructing the view of the ipsilateral true vocal cord. Symptoms depend on the site of origin. Most neurogenic tumors of the larynx originate in either the aryepiglottic fold or the false cord [63]. In these locations, the nerve of origin is likely to be the recurrent laryngeal nerve or the internal branch of the superior laryngeal nerve. As the tumor expands, it distorts the lateral larynx and eventually closes the airway and causes dysphonia. There are no characteristic features suggestive of neurilemoma on simple inspection, although CT and MRI can delineate between benign and malignant conditions in large tumors. The pathological diagnosis is dependent on three criteria: the presence of a capsule, identification of Antoni A and B areas, and a positive reaction of the tumor for S-100 protein.

7.9.1 Management

Ideally, a neurilemoma is totally excised, but anatomical constraints sometimes make this difficult. The preferred

method is microlaryngeal endoscopic excision with either conventional microlaryngeal endoscopic instrumentation or the use of CO_2 laser. The open approach may be necessary for large lesions. The treatment should be individualized with alternatives for an open approach via a transhyoid, laryngofissure or a lateral pharyngotomy approach.

7.10 Salivary Gland Tumors

Benign pleomorphic salivary adenoma (PSA) of the larynx has been reported more than 40 times [16], and another series of 11 cases was reviewed in the Japanese literature [64]. Males predominate slightly, with an age range from 15–82 years, with most cases presenting during the fifth to seventh decades. The type and severity of symptoms depends on the size and location of the tumor mass, with dysphonia and dyspnea symptoms being most common; some cases have been diagnosed en passant. The supraglottis is by far the commonest site, followed by the subglottis and the glottis (Fig. 7.11). Within the supraglottis the epiglottis is the most common site, located on the laryngeal surface most commonly. Only one case has involved the whole of one side of the larynx from the valleculae to the ventricle. The tumor presented as a mass with mucosal deformity without ulceration. The tumor may be pedunculated.

The differential diagnosis includes angioma, fibroma, cylindroma, lymphoma, schwannoma, aberrant thyroid, vestigial cyst, and internal laryngocele. Two cases have been reported in which the carcinoma arose in a pleomorphic adenoma within the larynx [45, 61].

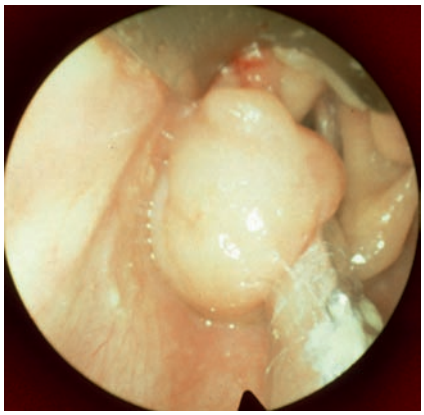

Fig. 7.11. Pleomorphic adenoma (salivary gland tumor) developed from the left supraglottis

7.10.1 Management

Surgical removal is curative and depends on the location and size of the tumor. Most of these lesions have been approached using a conservation surgical approach with curative intent. They have included endoscopic surgery including laser (Figs. 7.12 and 7.13) an external approach via a laryngofissure, or later pharyngotomy. However, if the tissue analyzed might be misinterpreted or an error made, a more extensive surgical approach may result; several such occasions have been reported. Importantly, the use of radiotherapy alone in a few cases did not shrink the tumor.

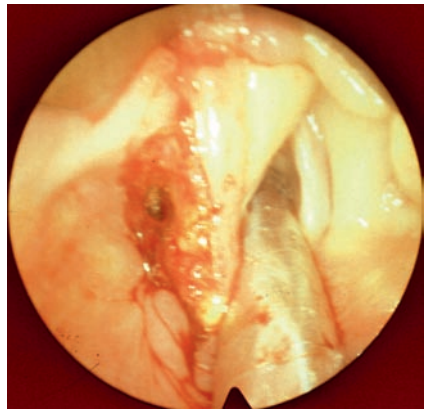

Fig. 7.12. Pleomorphic adenoma (salivary gland tumor) after endoscopic resection that had developed from the left supraglottis

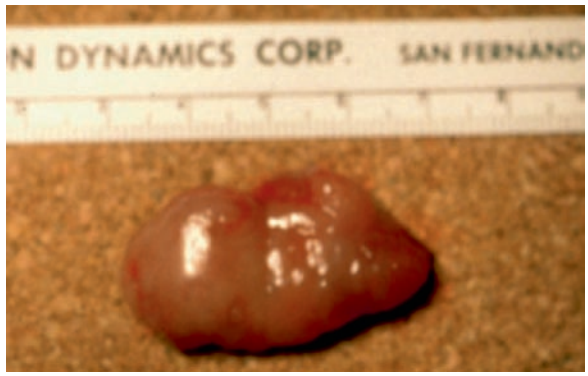

Fig. 7.13. Pleomorphic adenoma (salivary gland tumor) that had developed from the left supraglottis. Surgical specimen

7.11 Oncocytoma

Solitary oncocytomas are extremely rare, with few reported in the literature. Oncocytic hyperplasia, by contrast, is frequently diagnosed in elderly patients and is most commonly reported in the supraglottis [19]. Oncocytic lesions range from solid proliferation to a thin-walled cyst lined by multiple layers of cuboidal epithelium. Oncocytic lesions of the larynx manifest as a morphological spectrum of changes, including surface metaplasia of the respiratory or squamous epithelium, solitary oncocystic "adenomas" (neoplasms), multifocal "hyperplastic" masses, and cysts lined by oncocytes. Each of these entities is within the benign spectrum of oncocytic lesions without any treatment implications. However, oncocytic change/metaplasia can be diagnosed if it is present diffusely or multifocally throughout the larynx. If there is a solid proliferation of oncocytes, the designation "adenoma" can be used. Many cysts of the larynx are lined by oncocytes, and a clear distinction between saccular or ductal cyst and oncocystic papillary cystadenoma is not always possible.

7.11.1 Management

Endoscopic excision is curative [50]; it may be endoscopic, or a laryngofissure approach may be necessary. Recurrences have been reported and are most commonly associated with incomplete excision, although some may be associated with the development of a new lesion from a focus of oncocytic metaplasia previously undetected [19]. Surgery remains the treatment of choice for recurrent disease.

7.12 Necrotizing Sialometaplasia

Two cases of necrotizing sialometaplasia of the larynx have been reported. One case presented in the subglottis and the other in the false cord. It is suggested that this process is associated with other pathologies or processes. Hence, a secondary process occurring in the larynx at the same time or some other cause in the proximity should be sought, such as cancer. It is thought that the likely pathogenesis is vascular compromise of the affected area [73].

7.13 Paraganglioma

Neuroendocrine neoplasms of the larynx can be divided into two main groups: those of epithelial origin (carcinoid and neuroendocine carcinoma) and those of neural type (paraganglioma) [48]. Paragangliomas are uncommon, slow-growing, generally benign tumors. They arise from the paraganglion cells derived from the neural crest as part of a diffuse neuroendocrine system. To date, 76 cases have been identified as fulfilling the specific criteria laid down to make an accurate diagnosis.

In the larynx, there are two-paired paraganglia: the superior and inferior. The superior paraganglia are 0.1–0.3 mm in diameter and are situated in the false cord fold along the course of the superior laryngeal artery and nerve. The inferior paraganglia are 0.3–0.4 mm in diameter and are found near the lateral margin of the cricoid cartilage in the cricotracheal membrane along the course of the recurrent laryngeal nerve.

Typically, these tumors arise from the superior paraganglia (82%) and have a right-side, female predilection (3:1). Only 11 cases of subglottic paraganglia have been reported, again with a female preponderance. An uncommon case with a transventricular location and a fixed vocal cord presented a diagnostic challenge [25]. The age range is 5–90-plus years, although most laryngeal paragangliomas present during the fourth to sixth decades.

Examination reveals a red or blue lobulated, submucosal, smooth mass in the false cord. Rarely, it is associated with a neck mass, unless it is large enough to herniate through the thyrohyoid membrane. The lesion bleeds excessively if biopsied. It can be diagnosed with radiological imaging and angiography [62].

Histologically, paragangliomas are characterized by chief and sustentacular cells. Electron microscopy shows neural secretory granules. Chief cells stain positive for chromagranin and synaptophysin. The presence of mitotic activity does not correlate with the clinical behavior.

7.13.1 Management

The goal of treatment is eradication with preservation of maximal laryngeal function. Cryosurgery has been attempted, but laryngofissure or irradiation has been required following this procedure. No long term

follow-up of such cases has been documented. Endoscopic removal has been employed by several authors but has been associated with frequent recurrences. The successful use of CO_2 laser has been reported for a 4 × 4 × 3 cm mass in the supraglottis, with a postintubation period of 2 days, a protracted hospital stay, and a 5-year tumor-free follow-up [66]. Open surgery has in the past achieved excellent tumor control with preservation of laryngeal function, even when the tumor was located in the subglottis. Irradiation has not been reported as successful to date.

7.14 Granular Cell Tumors

Granular cell tumors are uncommon benign lesions that can appear anywhere in the body, although they have a predilection for the upper aerodigestive tract. In fact, 50% of all cases present in the head and neck region. The incidence of granular cell tumors in the larynx is 3–10% of cases in adults, and it is rare in children.

In the head and neck, the anterior tongue and the larynx are the first and second most common sites of these tumors [33, 71]. In the larynx, granular cell tumors are located on the posterior third of the vocal cord (Fig. 7.14). Symptoms depend on the location and size of the tumor, with the most common symptom being dysphonia; frequently, however, they are diagnosed in asymptomatic persons. The histopathological origin and etiology of this tumor are unknown.

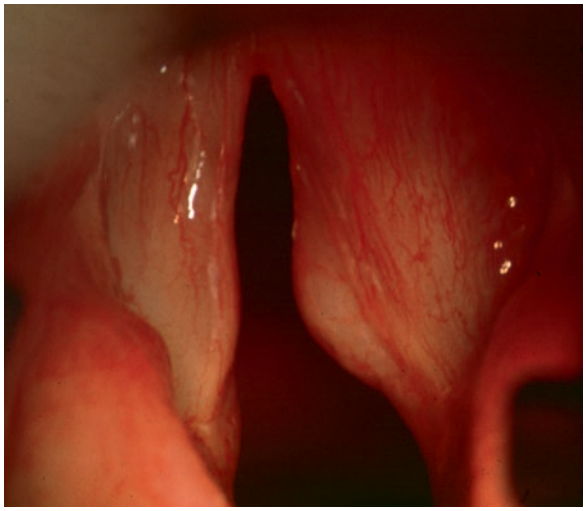

Fig. 7.14. Granular cell tumor in the posterior part of the right vocal fold

Macroscopically, these tumors are described as grayish-yellow, smooth but firm, well circumscribed, and polypoidal or sessile. As many as 50–65% of laryngeal granular cell tumors have pseudoepitheliomatous hyperplasia, which can lead to misinterpretation owing to the similarity of these lesions to squamous cell carcinoma. Granular cell tumors are not malignant, and malignant transformation has so far never been reported; laryngeal malignant granular cell tumors have been recorded, however. They metastasize early, and the prognosis is not good. A 34-year-old man, with a histologically benign granular cell tumor has been reported that recurred with rapid growth. The original tumor was characterized by atypia and pagetoid extensions into the epithelium. It is suggested that such cases be closely followed up. They should be distinguished from benign cases and should be suspected of behaving as a malignancy that has the potential to metastasize [8].

7.14.1 Management

Treatment is local excision by endoscopic, transoral, or laryngofissure methods appropriate to the site of the lesion. The recurrence rate after resection with free margins has been reported to be 8%, but this increases to 21–50% with positive margins. Frozen section analysis has been used to aid endoscopic excision with CO_2 laser and should be considered when there is pathological support for such a technique.

7.15 Giant Cell Tumors

The giant cell tumor is a true neoplasm and is presumed to be part of a series of tumors more frequently reported in long bones—the fibrohistiocytic series. In the larynx, giant cell tumors arise in the osteocartilaginous supporting structures of the larynx proper; they do not seem to be discrete soft tissue masses. One review suggested that 18 true cases have been reported [29]. The lesion involves men in their third to sixth decades; female patients have not been reported to date. Presenting problems include the presence of a slow-growing mass and dysphonia.

On examination, a mass is usually palpable, most commonly originating in the thyroid cartilage. Endoscopically, the lesions have proven to be deeply seated

with an intact overlying mucosa. CT scanning reveals a mass with a density intermediate between muscle and fat that may or may not show some central cystic change. The multinucleated giant cell type is more likely to show malignant features than the smaller mononuclear cell type. In all laryngeal giant cell tumors reported, however, tumors with both cell types have been cytologically benign.

7.15.1 Management

Early reports suggested that radiotherapy could be used to control these tumors. Modern therapy, however, suggests that either laryngectomy or hemilaryngectomy can achieve local control and obtain sufficient tissue to confirm the pathological diagnosis.

7.16 Chondroma

Laryngeal chondromas are uncommon and are seen most often during the sixth to seventh decades of life. The most frequent site is the cricoid, followed by the thyroid cartilage and, uncommonly, the epiglottis (Fig. 7.15) [4]. The exact number reported is unknown because it is difficult or impossible to distinguish a benign chondroma from a low-grade chondrosarcoma; it is suggested that the two patterns overlap, and a single tumor can exhibit both patterns. This may have occurred because of the small size of the biopsy specimen and may not be representative of the whole or entire tumor. It is therefore recommended that if a cartilage tumor is suspected the whole of the tumor be excised and subjected to histopathology. The treatment and prognosis of chondroma and low-grade chondrosarcoma is similar [32]. Should an excised chondroma recur, one should seriously doubt the accuracy of the initial diagnosis—it probably had been a low-grade chondrosarcoma all along.

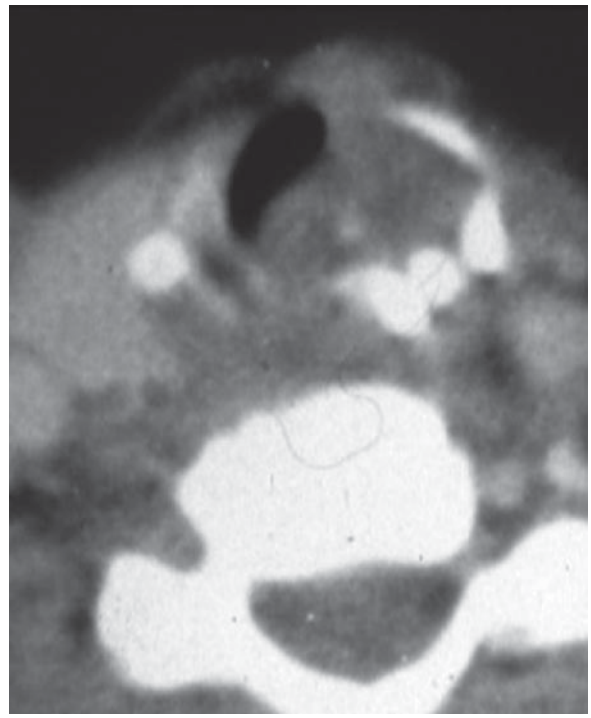

Fig. 7.15. Chondroma (low grade chondrosarcoma) that had developed from the cricoid cartilage. CT scan

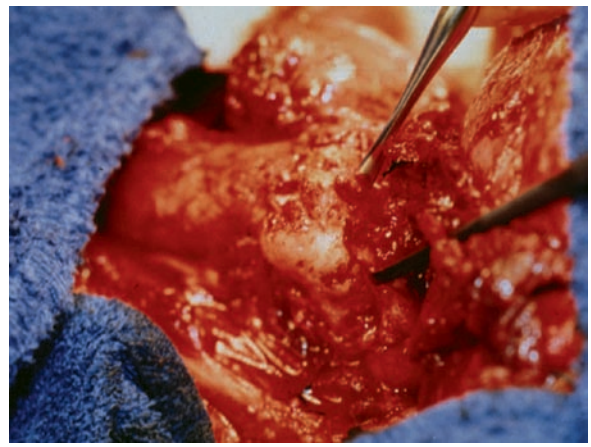

Fig. 7.16. Chondroma (low-grade chondrosarcoma) that had developed from the cricoid cartilage. Surgical view, open neck approach

7.16.1 Management

Surgery has always been the treatment of choice for laryngeal cartilage tumors. Most authors claim conservative surgery is the appropriate treatment for both low-grade tumors and chondromas. Even for cricoid lesions, conservative treatment through a laryngofissure is possible when the tumor involves less than half the cartilage. Radiotherapy for laryngeal cartilage tumors is controversial; the experience is limited to 12 cases, with only 2 cases of documented long-term follow-up (Fig. 7.16) [4]. Recent reports have described

CO_2 laser therapy as a procedure to deal with recurrences or even the primary lesion [60, 77].

7.17 Nonneoplastic Laryngeal Tumors

7.17.1 Hamartomas

According to the World Health Organization (WHO) classification, a hamartoma is a "developmental anomaly characterised by the formation of a tumor-like mass composed of mature tissue elements that are normally present in the location where it is found but occurring in abnormal proportions or arrangements" [78]. Hamartomas of the head and neck are uncommon but have been described in the sinonasal tract, nasopharynx, oral cavity, oropharynx, larynx hypopharynx, cervical esophagus, ear, parotid gland, trachea, parathyroid gland, and eye. They may be unifocal or multifocal. The term "pleiotropic hamartoma" is used to indicate the presence of multiple hamartomas at different sites in a given patient. Hamartomas of the larynx are rare [59]. Presently, it appears that there are only 11 cases of well documented hamartoma of the larynx. Males are more involved than females, with age peaks during early childhood and middle age (39–56 years). Of the 11 cases accepted as hamartomas of the larynx, 6 of the patients were 16 years of age or older. The main symptoms of laryngeal involvement are similar to those of other benign mass lesions: dysphonia, dyspnea, and dysphagia.

Microscopically, the tissues show a disorganized architectural pattern with mesenchymal derivatives alone or with superadded epithelial elements. Hamartomas of the larynx are mainly composed of cartilage and fibromuscular tissue. Fatty tissue and nerve elements are often seen. No features of malignancy are present. The dominant tissue defines the lesion (e.g., cartilage hamartoma or myxochondromatous hamartoma). Such lesions must be differentiated from choristoma, teratoma, and rhabdomyoma, among others.

7.17.1.1 Management

Treatment consists of local excision, with recurrences usually associated with incomplete removal.

7.18 Pseudotumors or Pseudoneoplastic Lesions

From a practical point of view, pseudoneoplastic lesions of the larynx may be divided broadly into two groups: (1) growths that present clinically as mass lesions but by histological examination are readily diagnosed and are appropriately classified as benign nonneoplastic lesions; and (2) benign lesions that may show histopathological features suggestive of neoplasia. The latter group may be further divided into lesions that are *clinically* suspicious and those that present a *microscopic* dilemma [74]. Some are discussed below.

7.19 Inflammatory Fibroblastic Tumors

Inflammatory myofibroblastic tumors (IMTs) can be polypoid, pedunculated, spherical, lobular, or nodular, with a smooth external appearance. They may be confined to the immediate submucosal region and not truly invading any tissue. They are firm in consistency, fleshy and gritty on cut surface, gray-yellow or tan-white, and may measure up to 3 cm in greatest dimension. To date, only 10 IMTs have been reported in the larynx [24].

The most common site is the vocal cord [17]. These lesions are usually located on the true vocal cord, although the subglottis and upper trachea can be involved. The lesions may have a myxomatous appearance, but they do not exhibit necrosis or hemorrhage. Special histopathological stains confirm the diagnosis. The differential diagnosis centers around spindle cell squamous cell carcinoma, but inflammatory fibrosarcoma, nerve sheath tumors, nodular fasciitis, and nonspecific inflammation must be also excluded [41].

7.19.1 Management

Surgical excision is the treatment of choice [24] but may have to be repeated frequently before the correct diagnosis is confirmed [43].

7.20 Fibroma

Fibromas generally present as polyps or nodules, sessile or pedunculated, and soft or firm; their size depends on the duration and intensity of exposure to the irritating factors. Most lesions are covered by intact epithelium, often exhibiting keratosis, and can measure up to 4 cm. Many fibromas involve Reinke's space (superficial lamina propria) and arise from the anterior two-thirds of the vocal cord. Fibromas probably represent a reactive change and are not true neoplasms. With removal of the putative underlying insult, healing may occur after surgical excision. All lesions removed from the larynx require histopathological examination, with a diagnosis being essential for patient management and prognosis.

7.21 Amyloidosis

Isolated amyloidosis (without plasmactoma) frequently occurs along the false vocal cord, although any portion of the larynx can be affected. The term amyloidosis is used to indicate an extracellular accumulation of homogeneous protein-derived fibrillary and eosinophilic material, with well defined histochemical characteristics. When amyloidosis involves the supraglottic or glottic region, the lesion demonstrates an elevated, smooth or bosselated, polypoidal, mucosa-covered, firm mass. Subglottic amyloidosis presents as a more generalized, diffuse swelling. Multifocal deposits occur quite frequently. Surface ulceration has been reported in more extensive and larger lesions. The mass is firm, with a waxy, translucent cut surface ranging in color from tan-yellow to red-gray [75]. It is reported that up to 15% of patients who demonstrate laryngeal amyloidosis may have amyloid deposits at other head and neck sites.

It is important that when diagnosed with amyloidosis the patient is screened for the possibility that he or she may have tumor-forming amyloid, primary systemic amyloidosis (diagnosed by serum or urine immunoelectrophoresis or by rectal biopsy), secondary amyloidosis (associated with some other predisposing disease), or plasmacytoma, whether it be solitary or part of multiple myeloma. The most common amyloid lesion seen in the larynx is amyloid deposition alone, a localized amyloid deposit, or an amyloid tumor (without associated lymphoproliferative disorder) [55].

7.21.1 Management

Most authors agree that surgery should be the treatment of choice of laryngeal amyloidosis. Surgical procedures include external partial laryngectomy or microlaryngeal excision. An alternative technique is the use of CO_2 laser excision [41].

7.22 Laryngeal Cysts

The gross appearance of cysts in the larynx is often determined by the point of origin in the larynx and the type of cyst (saccular, retention/inclusive, ductal, vascular, traumatic). The cyst can be considered external or internal to the larynx based on the degree of compression of the larynx by the cyst and the extent of the disease in the larynx. Cysts generally do not communicate with the interior of the larynx. A laryngocele (air-filled herniation or dilation of the saccule) can be internal or external to the larynx, communicating with the lumen (Fig. 7.17–7.20). Saccular cysts (anterior or lateral) are submucosal and do not communicate with the lumen but, instead, are filled with mucus or acute inflammatory elements.

Cysts occur in all regions of the larynx, with retention cysts most often located in the epiglottis, saccular cysts in the false cord, and traumatic cysts in the

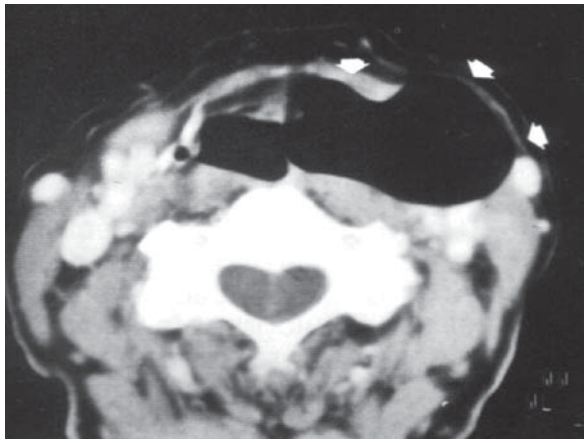

Fig. 7.17. External laryngocele. CT scan

Fig. 7.18. External laryngocele

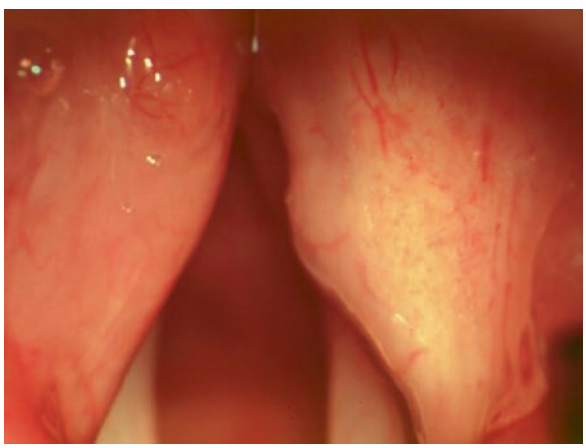

Fig. 7.19. Internal laryngocele that had developed in the right ventricular fold

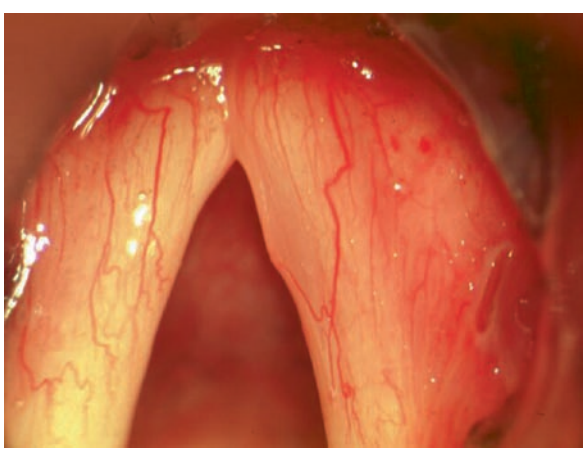

Fig. 7.20. Internal laryngocele that had developed in the right ventricular fold. After endoscopic resection

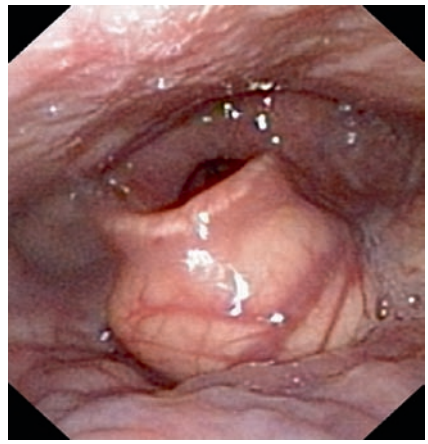

Fig. 7.21. Retentional cyst in the lingual side of the epiglottis

arytenoid region. The size of the cyst depends on the location; small cysts are usually found on the vocal cords, whereas large cysts are found attached to the epiglottis, pushing the larynx to one side, or projecting into the hypopharynx (Fig. 7.21).

Cyst walls, consisting of fibrous connective tissue, vary in thickness. The lining helps differentiate the cysts into a variety of subtypes. Most cysts are lined by squamous or respiratory epithelium (retention and saccular), and a few cysts are lined by fibrous connective tissue. Those with an admixture of mesodermal and endodermal layers qualify as congenital or embryonal cysts. It has been proposed that all laryngeal cysts can be classified into congenital, retention, and inclusion cysts [3].

7.22.1 Management

All cysts should be considered for a histopathological diagnosis. A biopsy should confirm the clinical suspicion before reassurance is given.

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References

1. Anderson TD, Weinstein GS (2000) Recurrent angiomyoma (vascular leiomyoma) of the larynx after laser excision. Otolaryngol Head Neck Surg 123(5):646–647

2. Andrus JG, Shapshay SM (2006) Contemporary management of laryngeal papilloma in adults and children. Otolaryngol Clin North Am 39(1):135–158
3. Arens C, Glanz H, Kleinsasser O, et al (1997) Clinical and morphological aspects of laryngeal cysts. Eur Arch Oto-Rhino-Laryngol 254(9–10):430–436
4. Baatenburg de Jong RJ, van Lent S, Hogendoorn PCW (2004) Chondroma and chondrosarcoma of the Larynx. Curr Opin ORL-HNS 12:98–105
5. Barnes L (2001) Diseases of the larynx, hypopharynx, and oesophagus. In: Textbook surgical pathology of the head and neck, Chapter 5, 2nd ed. revised and expanded, in Chapter 1. New York/Basel, Marcel Dekker, pp. 151–154
6. Barnes L, Ferlito A (1993) Soft tissue neoplasms. In: Ferlito A (ed.) Neoplasms of the larynx. 1st ed.Churchill Livingstone, Hong Kong, pp. 630–638
7. Bradley PJ, Narula AA, Harvey L, et al (1989) Haemangiopericytoma of the larynx. J Laryngol Otol 103(2):234–238
8. Brandwein M, LeBenger J, Strauchen J, et al (1990) Atypical granular cell tumor of the larynx: an unusually aggressive tumor clinically and microscopically. Head Neck 12:154–159
9. Brys AK, Sakai O, DeRosa J, et al (2005) Rhabdomyoma of the larynx: case report and clinical and pathologic review. Ear, Nose Throat J 84(7):437–440
10. Chau HN,Desai K, Georgalas C, et al (2005) Variability in nomenclature of benign laryngeal pathology based on video laryngoscopy with and without stroboscopy. Clin Otolaryngol 30(5):424–427
11. Chhetri DK, Blumin JH, Shapiro NL, et al (2002) Office-based treatment of laryngeal papillomatosis with percutaneous injection of cidofovir. Otolaryngol Head Neck Surg 126(6):642–648
12. Clyne SB, Halum SL, Kaufman JA, et al (2005) Pulsed dye laser treatment of laryngeal granulomas. Ann Otol Rhinol Laryngol 114(3):198–201
13. Derkay CS (1995). Task force on recurrent respiratory papillomas. A preliminary report. Arch Otolaryngol 121(12): 1386–1391
14. Derkay CS (2001) Recurrent respiratory papillomatosis. Laryngoscope 111(1):57–69
15. Dikkers FG (2006) Treatment of recurrent respiratory papillomatosis with microsurgery in combination with intralesional cidofovir--a prospective study. Euro Arch Oto-Rhino-Laryngol 263(5):440–443
16. Dubey SP,Banerjee S, Ghosh LM, et al (1997) Benign pleomorphic adenoma of the larynx: report of a case and review and analysis of 20 additional cases in the literature. Ear Nose Throat J 76(8):548–557
17. Ereno C, Grande J, Santaolalla F, et al (2001) Inflammatory myofibroblastic tumor of the larynx. J Laryngol Otol 115: 856–858
18. Ferguson GB (1944) Hemangioma of the adult and infant larynx: a review of the literature and a report of 2 cases. Arch Otolaryngol Head Neck Surg 40:189–195
19. Ferlito AA, Recher G (1981). Oncocytic lesions of the larynx. Arch Otorhinolaryngol 232(2):107–115
20. Franco RA Jr, Zeitels SM, Farinelli WA, et al (2002) 585-nm pulsed dye laser treatment of glottal papillomatosis. Ann Otol Rhinol Laryngol 111(6):486–492
21. Gerein V, Rastorguev EE, Gerein J, et al (2005). Incidence, age at onset, and potential reasons of malignant transformation in recurrent respiratory papillomatosis patients: 20 years experience. Otolaryngol Head Neck Surg 132(3):392–394
22. Gerein V, Rastorguev E, Gerein J, et al (2005). Use of interferon-alpha in recurrent respiratory papillomatosis: 20-year follow-up. Anna Otol Rhinol Laryngol 114(6):463–471
23. Glanz H, Schulz A, Kleinsasser O, et al (1997) Benign lesions of the larynx: basic clinical and histopathological data. In: Kelinsasser O, Glanz H, and Olofsson J (eds) Advances of laryngology in Europe. Elsevier, Amsterdam, pp. 3–14
24. Guilemany JM, Alos L, Alobid I, et al (2005) Inflammatory myofibroblastic tumor in the larynx: clinicopathological features and histeogenesis. Acta Otolaryngol 125(2):215–219
25. Gupta S, Pathak KA, Sanghvi V (2003) Transventriular paraganglioma of the larynx. Eur Arch Otorhinolaryngol 260(7):358–360
26. Haglund S, Lundquist PG, et al (1981) Interferon therapy in juvenile laryngeal papillomatosis. Arch Otolaryngol 107(6): 327–332
27. Hammermann H, Glanz H, Kleinsasser O (1997) Lipomas of the larynx and hypopharynx: possible transformation into well-differentiated liposarcomas. In: Kelinsasser O, Glanz H, Olofsson J (eds) Advances of laryngology in Europe. Elsevier, Amsterdam, pp. 87–90
28. Healy GB, Gelber RD, Trowbridge AL, et al (1988) Treatment of recurrent respiratory papillomatosis with human leukocyte interferon. Results of a multicenter randomized clinical trial. N Eng J Med 319(7):401–417
29. Hinni ML (2000) Giant cell tumor of the larynx. Ann Otol Rhinol Laryngol 109:63–66
30. Holinger PH, Johnston KC (1951) Benign tumors of the larynx. Ann Otol Rhinol Laryngol 60(2):496–509
31. Jensen K, Swartz K (2006) A rare case of rhabdomyoma of the larynx causing airway obstruction. Ear Nose Throat J 85(2): 116–118
32. Jines DA, Dillard SC, Bradford CR, et al (2003) Cartilage tumors of the larynx. J Otolaryngol 32(5):332–337
33. Johansen EC, Illum P (1995) Rhabdomyoma of the larynx: a review of the literature with a summary of previously described cases of rhabdomyoma of the larynx and a report of a new case. J Laryngol Otol 109(2):147–153
34. Jungehulsing M, Fishbach R, Pototschnig C, et al (2000) Rare benign tumors: laryngeal and hypopharyngeal lipomata. Ann Otol Rhinol Laryngol 109:301–305
35. Kapur TR (1968) Recurrent lipomata of the larynx and the Pharynx with late malignant change. J Laryngol Otol 82: 761–768
36. Kawakami M, Hayashi I, Yoshimura K, et al (2006) Adult giant hemangioma of the larynx. Auris, Nasus Larynx 33:479–482
37. LaBagnara J, Hitchcock E, Spitzer T (1999) Rhabdomyoma of the true vocal fold. J Voice 13(2):289–293
38. Leventhal BG, Kashima HK, Mounts P. et al (1991) Long-term response of recurrent respiratory papillomatosis to treatment with lymphoblastoid interferon alfa-N1. Papilloma Study Group. N Eng J Med 325(9):613–617
39. Liang GS, Loevner LA, Kumar P (2000) Laryngeal rhabdomyoma involving the paraglottic space. Am J Radiol 174: 1285–1387
40. Liess BD, Zitsch RP, Lane R, et al (2005) Multifocal adult rhabdomyoma: a case report and literature review. Am J Otolaryngol 26:214–217
41. Lucioni M, Marioni G, Libera DD, et al (2006) Adult laryngeal hemangioma CO_2 laser excision. Acta Otolaryngol 126: 621–626

42. MacGregor AR, Batsakis JG, El-Naggar AK (2003) Myofibroblastoma of the larynx: a study of two cases. Head Neck 25:606–611
43. Martines F, Martines E, Caamitjana CF, et al (2007) Inflammatory myofibroblastic tumor of the larynx: Case report. An Otorhinolaringol Ibero Am. 34(2):210–208
44. Michaels L, Hellquist HB (2001) Textbook: ear nose and throat histopathology. Springer, London
45. Milford CA, Mulgliston TA, O'Flynn P, et al (1989). Carcinoma arising in a pleomorphic adenoma of the epiglottis. J Laryngol Otol 103:324–327
46. Motta G, Salzano FA, Motta S, et al (2003) CO_2 - laser treatment of laryngeal amyloidosis. J Laryngol Otol 117:647–650
47. Myer CM, 3rd, Willging JP, McMurray S, et al (1999) Use of a laryngeal micro resector system. Laryngoscope 109(7 Pt 1): 1165–1166
48. Myssiorek D, Rinaldo A, Barnes L, et al (2004). Laryngeal paraganglioma: an update critical review. Acat Otolaryngol 124:995–999
49. Nappi O, Ritter JH, Pettinato G, et al (1995) Haemangiopericytoma: histopathological pattern or clinicopathologic entity? Semin Diagn Pathol 12(3):221–232
50. Narozny WB, Mikaszewski B, Stankiewicz C (1995) Benign neoplasms of the larynx. Auris Nasus Larynx 22(1):38–42
51. New GB, Erich JB (1938) Benign tumors of the larynx: a study of 722 cases. Arch Otolaryngol Head Neck Surg 28:841
52. Newton JR, Ruckley EW, Earl UM (2006) Laryngeal neurilemmoma: a case report. Ear, Nose Throat J 85:448–449
53. Pelucchi, S, Amoroso C, Grandi E, et al (2002) Granular cell tumor of the larynx: Literature review and case report. J Laryngol 31:234–235
54. Pontes P, Avelino M, Pignatari S, et al (2006) Effect of local application of cidofovir on the control of recurrences in recurrent laryngeal papillomatosis. Otolaryngol Head Neck Surg 135(1):22–27
55. Popella C, Glanz H, Kelinsasser O, et al (1997) Various clinical and pathomorphological appearances on amyloid deposits in the larynx. In: Kelinsasser O, Glanz H, Olofsson J (eds) Advances of laryngology in Europe. Elsevier, Amsterdam, pp. 53–55
56. Reeves WC, Ruparelia SS, Swanson KI et al (2003) National registry for juvenile-onset recurrent respiratory papillomatosis. Arch Otolaryngol Head Neck Surg 129(9):976–982
57. Reidy PM, Dedo HH, Rabah R, et al (2004) Integration of human papillomavirus type 11 in recurrent respiratory papilloma-associated cancer. Laryngoscope 114(11):1906–1909
58. Rihkanen H, Aaltonen LM, Syrjanen SM (1993) Human papillomavirus in laryngeal papillomas and in adjacent normal epithelium Clin Otolaryngol 18(6):470–474
59. Rinaldo A, Fisher C, Mannara GM, et al (1998) Hamartoma of the larynx: a critical review of the literature. Ann Otol Rhinol Laryngol 107:264–267
60. Rinaldo A, Howard DJ, Ferlito AA (2000) Laryngeal chondrosarcoma: a 24 year experience at the Royal National Throat, Nose and Ear Hospital. Acta Otolaryngol 120:680–688
61. Sabri JA, Hajjar MA (1967) Malignant mixed tumor of the vocal cord. Arch Otolaryngol 85:118–120
62. Sanders KW, Abreo F, Rivera E (2001) A diagnostic and therapeutic approach to paragangliomas of the larynx. Arch Otolaryngol Head Neck Surg 127(5):565–569
63. Sanghvi V, Lala M, Borges A, Rodrigues G, Pathak KA, Parikh D (1999). Lateral thyrotomy for neurilemmoma of the larynx. J Laryngol Otol 113:346–348
64. Sawatsubashi M, Tuda K, Tokunaga O, et al (1997). Pleomorphic adenoma of the larynx: a case report and a review of the literature in Japan. Otolaryngol Head Neck Surg 117(4):415–417
65. Schraff S, Derkay CS, Burke B, et al (2004). American Society of Paediatric Otolaryngology members' experience with recurrent respiratory papillomatosis and the use of adjuvant therapy. Arch Otolaryngol Head Neck Surg130(9): 1039–1042
66. Sesterhenn AM, Folz BJ, Lippert BM, et al (2003). Laser surgery treatment of laryngeal paraganglioma. J Laryngol Otol 117(5):641–646
67. Shehab N, Sweet BV, Hogikyan ND (2005) Cidofovir for the treatment of recurrent respiratory papillomatosis: a review of the literature. Pharmacotherapy 25(7):977–989
68. Snoeck R,Wellens W, Desloovere C, et al (1998). Treatment of severe laryngeal papillomatosis with intralesional injections of cidofovir [(S)-1-(3-hydroxy-2-phosphonylmethoxypropyl) cytosine]. J Med Virol 54(3):219–225
69. Syeda F, Hussain A (2005) Schwannoma of the larynx: A case report. Ear, Nose Throat J 84(11):732–734
70. Taylor J, Stiefel M, Park SY (2006) Schwannoma of the true vocal fold: A rare diagnosis. Ear, Nose Throat J 85(1): 52–53, 59
71. Toprak M, Oz F, Oktem F, Acioglu E, et al (2003). Granular cell tumor of the larynx. J Otolaryngol 34:363–365
72. Van Cutsem E, Snoeck R, Van Ranst M, et al (1995) Successful treatment of a squamous papilloma of the hypopharynx-esophagus by local injections of (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine. J Med Virol 45(2):230–235
73. Wenig BM (1995) Necrotising sialometaplasia of the larynx. Am J Clin Pathol 103(5):609–613
74. Wenig BM, Devaney K, Bisceglia M (1995) Inflammatory myofibroblastic tumor of the larynx. Cancer 76(11): 2217–2229
75. Wenig BM, Devaney K, Wenig BL (1995). Pseudoneoplastic lesions of the oropharynx and larynx simulating cancer. Pathol Annu 30(pt 1):143–187
76. Wiatrak BJ, Wiatrak DW, Broker TR et al (2004). Recurrent respiratory papillomatosis: a longitudinal study comparing severity associated with human papilloma viral types 6 and 11 and other risk factors in a large pediatric population. Laryngoscope 114(11 Pt 2 Suppl 104):1–23
77. Windfuhr JP (2003). Pitfalls in the diagnosis and management of laryngeal chondrosarcoma. J Laryngol Otol 117: 651–655
78. World Health Organisation (1991). Histological typing of tumors of the upper respiratory tract and ear. Springer-Verlag, Berlin
79. Yilmaz MD, Aktepe F, Altuntas A (2004). Cavernous hemangioma of the left vocal cord. Eur Arch Otorhinolaryngol 261: 310–311
80. Yellin S, LaBruna A, Ananol VK et al (1996). Nd: YAG laser treatment for laryngeal and hypopharyngeal hemangiomas: A new technique. Ann Otol Rhinol Laryngol 105:510–515