Larynx: Malignant Tumors

LARYNX, HYPOPHARYNX, AND CERVICAL ESOPHAGUS

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KEY POINTS

- CT and MRI are important tools for establishing the entire extent of a primary laryngeal cancer much of which that is often beyond endoscopic detection in locally advanced cancers
- CT and MRI are important tools for establishing the extent of cervical and retropharyngeal lymph node metastases
- These two factors help determine optimal treatment strategies
- FDG PET used judiciously can further aid this diagnostic process
- Surveillance imaging can be by a combination of anatomic and/or radionuclide imaging- the best strategies are individualized to each particular patient's circumstances
- CT and MRI are important tools for differentiating radionecrosis of the laryngeal skeleton from recurrence and determining the possible threat of radionecrosis to airway integrity

INTRODUCTION

Staging and medical decision-making procedures for laryngeal cancer include indirect laryngoscopy, direct laryngoscopy with biopsy, contrast-enhanced computed tomography (CECT) or contrast-enhanced magnetic resonance (CEMR) depending on the practice preference, and a chest x-ray. Imaging studies are an essential component of the clinical diagnostic evaluation, providing unique and often pivotal information that complements the clinical examination. Imaging provides additional information concerning the deep extent and regional spread of disease. Chest computed tomography (CT) and fluorine-18 2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) may provide additional information in selected cases.

This chapter describes the important role of diagnostic imaging in clinical decision making for laryngeal cancer. Squamous cell carcinoma (SCCA), the most common malignancy, is considered in the first section, and the less common malignant tumors are presented in the second section.

ANATOMIC AND DEVELOPMENTAL CONSIDERATIONS

Applied Anatomy

A thorough knowledge of laryngeal anatomy and anatomic variations in each of the following areas is required for the evaluation of laryngeal malignant tumors. This anatomy is presented in detail in the following introductory chapters:

Primary Site Evaluation

- Larynx, including the laryngeal skeleton, deep tissues spaces within the larynx, mucosal landmarks, and functional structures within the larynx (Chapter 201)
- Hypopharynx (Chapter 215)
- Tongue base region and low oropharyngeal wall (Chapter 190)
- Cervical esophagus, including the critical esophageal verge at the junction of the postcricoid portion of the hypopharynx and cervical esophagus (Chapter 221)
- Trachea (Chapter 209)

Evaluation of Extralaryngeal Spread

- Visceral compartment of the neck and related fasciae (Chapter 149)

Evaluation of Regional Lymph Nodes Disease

- Detailed knowledge of normal node and perinodal morphology and the common drainage pathways of laryngeal cancer, which emphasizes nodal levels 2 through 6 (Chapters 149 and 157)

Evaluation of Perivascular and Perineural Spread

- Knowledge of the entire course of the vagus and recurrent laryngeal nerves on both sides and of the superior and inferior laryngeal neurovascular bundle (Chapter 201)

IMAGING APPROACH

Techniques and Relevant Aspects

Specific CT and magnetic resonance (MR) techniques for study of the larynx are reviewed in Chapter 201, and specific protocols for laryngeal malignant tumors and related problems are presented in Appendixes A and B. A few points of emphasis related to malignant laryngeal tumors follow. The neck should always be slightly hyperextended for laryngeal CT to reduce shoulder-related artifacts. Laryngeal images must be viewed as parallel to the true vocal cords (TVCs). Sections made or viewed oblique relative to the TVC can produce substandard images that lead to interpretative difficulties. In particular, review of skewed images may lead to an errant interpretation of the anatomic relationships in the transglottic region that are often critical to medical decision making.

Intravenous contrast must be used for all studies of laryngeal cancer unless there is a compelling contraindication. Many primary tumors will enhance, improving the tumor-to-muscle contrast, and intravenous contrast use is critical in the evaluation of altered nodal morphology and likely perfusion as an indication of metastasis. If iodinated contrast cannot be used, then magnetic resonance imaging (MRI) should be considered as the primary study for any lesion except a limited glottic cancer. The use of intravenous paramagnetic contrast is individualized, but generally it is necessary.

Pros and Cons

Indications for Study

Evaluation of the Primary Site and Regional Disease

T1 lesions of the TVC do not usually require imaging. Any tumor that is suspicious for deep infiltration should be studied primarily with CT (Fig. 206.1). Supplemental MR study is directed by CT findings to a localized area of interest where its strengths related to better soft tissue contrast resolution may be exploited (Fig. 206.2). A large proportion of MR studies will be of poor quality owing to motion artifacts.

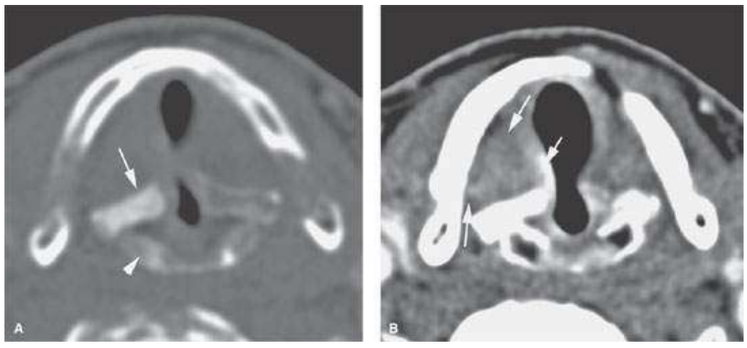
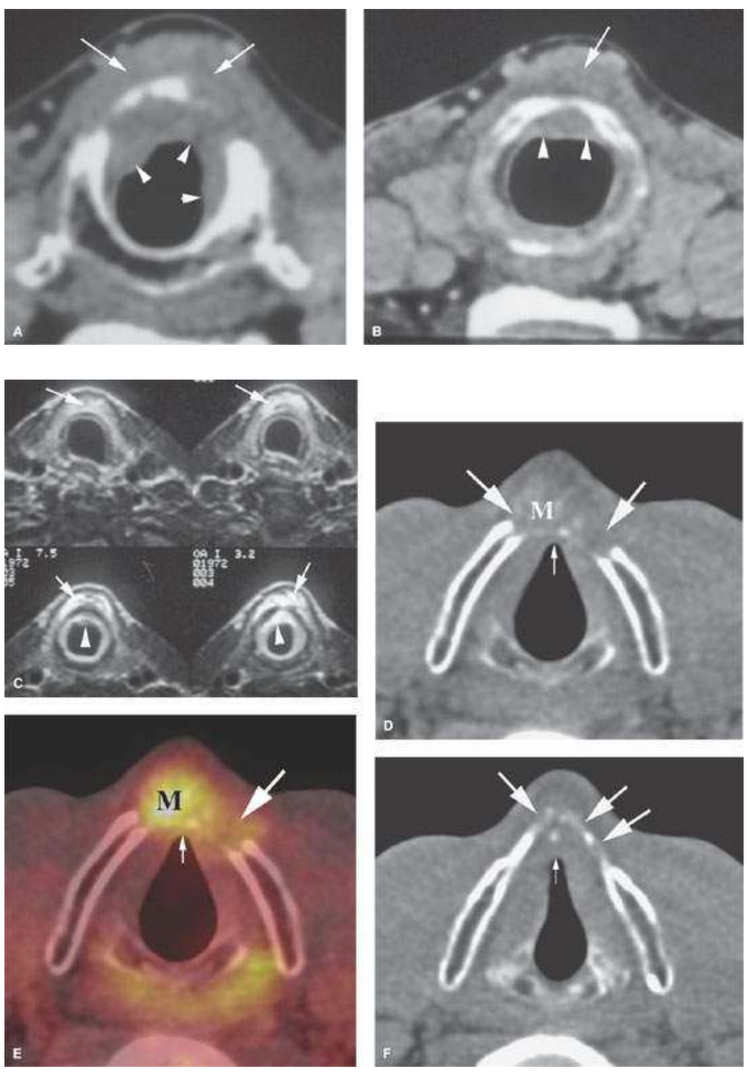


FIGURE 206.1. A patient with irregularity of the right true vocal cord noted clinically. Computed tomography study in (A) shows a sclerotic arytenoid (arrow) and top of the cricoid cartilage (arrowhead). These findings are suspicious for at least chronic inflammation and likely adjacent tumor. Multiple biopsies showed only dysplasia. The patient was re-biopsied, and carcinoma was diagnosed. In (B), the vocal cords are apposed because the patient was holding his breath. There was slight bulge of the posterior cord and some thickening of the true cord, but the paraglottic fat is preserved. Findings were consistent with a very limited superficial lesion. The patient responded completely to radiotherapy.

All primary tumors must be evaluated for the extent of the endolaryngeal spread of the primary; cartilage invasion; spread to adjacent structures including the hypopharynx, tongue base, trachea, and esophagus; and extralaryngeal spread to the soft tissues of the neck. The evaluation must also include a search for regional adenopathy and spread along neurovascular bundles at risk. Finally, the risk of any acute adverse complication should be anticipated, such as the lesion really representing one of vascular origin that would not be optimal for a deep biting type of tissue sampling.

There are several areas where CT or MR images consistently provide better information than the endoscopic examination. These include spread to the subglottis, paraglottic space, pre-epiglottic space, tongue base via the pre-epiglottic space, and cartilage invasion. These imaging studies also allow tumor volumes that may reside in these deep spaces to be measured along with the more exophytic component.



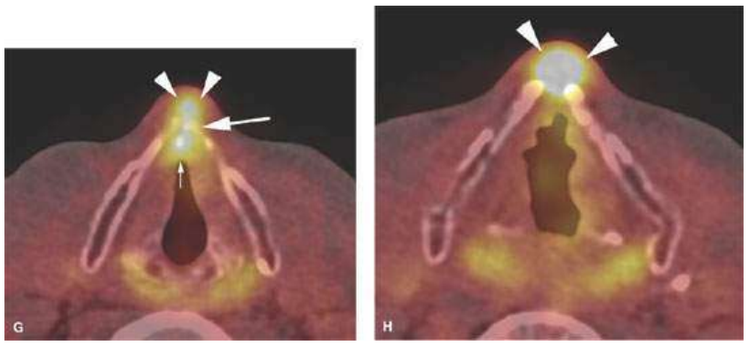


FIGURE 206.2. A–C: Patient 1 with subglottic carcinoma. The computed tomography (CT) images in (A) and (B) show the endoluminal portion of the tumor (arrowheads) but also show spread of tumor anterior to the cricoid cartilage (arrows). In (C), the magnetic resonance images again clearly show the endoluminal component (arrowheads) but also more definitely demonstrate the tumor spreading beneath the infrahyoid strap muscles (arrows) so low that the tracheostomy in this patient had to be placed lower than usual. D–H: Patient 2 with an fluorine-18 2-fluoro-2-deoxy-D-glucose positron emission tomography (PET–FDG) study that graphically depicts cartilage invasion and extralaryngeal spread of tumor but contributes no additional information that substantively changes the approach to treatment that would be based on the anatomic images. A non–contrast-enhanced axial CT image at the level of superior cricoid cartilage (D) demonstrates mild thickening of the anterior commissure (small white arrow) and gross destruction of the thyroid cartilage bilaterally (large arrows) that is caused by a heterogeneous-appearing mass (M). The mass grossly infiltrates the prelaryngeal soft tissues. The fused axial PET CT image at the same level (E) shows markedly increased FDG uptake in the heterogeneous-appearing mass (M) and slightly increased FDG uptake at the anterior commissure (small white arrow) and site of thyroid cartilage destruction (large arrow). The non–contrast-enhanced axial CT image at the level of the arytenoids cartilages (F) shows persistent marked thickening of the anterior commissure (small white arrow). The anterior portions of the thyroid cartilage bilaterally (large arrows) are present but markedly less mineralized in nature than the remaining portions of the thyroid cartilage. Since no mass is seen at this level, it is unclear if the patchy mineralization is caused by tumor infiltration or represents physiologic variation in thyroid cartilage mineralization.

Detection of Recurrent Tumor

Diagnostic CT is the examination for detection of recurrence in the neck, study of the neopharynx, or the irradiated larynx; in selected cases, positron emission tomography (PET) may be useful, as discussed in the subsequent section on follow-up surveillance.

Evaluation of Laryngeal Dysfunction and Submucosal Masses

Some patients have SCCAs growing entirely beneath intact mucosa. These malignancies may begin on the mucosa within the laryngeal ventricle and the false vocal cord (FVC) and grow in the paraglottic space (Fig. 6.3). Submucosal masses caused by an enchondroma or chondrosarcoma are more specifically diagnosed by CT than MRI (Figs. 205.6 and 205.7 and Chapter 39). Other submucosal cancers from minor salivary and benign mesenchymal tumors cannot be distinguished from SCCAs (Chapter 205). A rare paraganglioma might be anticipated by intense vascularity and an enlarged superior laryngeal vascular bundle (Fig. 205.2). About half of all submucosal laryngeal masses will be laryngoceles. The presence of a laryngocele requires a search for an obstructing primary tumor (Chapter 203). Deformity of the laryngeal skeleton due to old trauma or developmental variations may cause laryngeal dysfunction and a mucosal bulge. This condition is readily recognized (Figs. 201.35, 201.36, and 205.7E and Chapter 201). All of these conditions that may produce a submucosal laryngeal mass are discussed in more detail elsewhere.

Dysphonia, Vocal Cord Dysfunction, and Palsy

TVC dysfunction that is believed clinically to be due to recurrent laryngeal or vagal neuropathy will on occasion be caused by an entirely submucosal laryngeal pathology; the most frequent cause is cancer (Fig. 206.3).

CT is the preferred imaging modality since it not only provides a good evaluation of the larynx but also can easily be extended to include the upper thoracic cavity or intracranial structures when the cause is not endolaryngeal, as discussed in Chapter 201. Adjunctive MRI may be used selectively to evaluate the cisternal course of the vagus nerve and its brain stem nuclei.

Controversies

Cartilage Invasion

CT and MR vastly improve the clinical detection of subtle cartilage invasion. A slice thickness, 3 mm (preferably 0.5 to 1.0 mm) is required for this task, so CT is the better choice as the primary examination. There have been suggestions that MR is better than CT for detection of early cartilage invasion. CT and MR are both imperfect in detecting early macroinvasion and, of course by definition, cannot directly show microinvasion. Variation in ossification of the cartilages and the related marrow spaces makes interpretation difficult. Volume averaging aggravates the effects of these anatomic variations. Foci of cartilage/bone invasion .3 to 5 mm should be visible or strongly suggestive of early macroinvasion if imaging techniques are adequate. CT sections, 3 mm thick and reformations facilitate the search for small defects and early marrow space invasion (Fig. 206.4).

The contrast resolution of MR can show small areas of marrow space invasion. Unfortunately, replacement of fat in the marrow space of the thyroid cartilage can be due to reactive fibrovascular proliferation, caused by a tumor adjacent to but not invading the cartilage in question1 (Fig. 206.5). This leads to false-positive interpretation of both CT and MR studies as suggesting minimal macro- or microinvasion. Such false-positive readings may lead to unwarranted upward stage migration, since tumors with thyroid cartilage invasion are designated as T4 tumors. More importantly, it could cause needless loss of the larynx in the hands of those not thoroughly familiar with these pitfalls and limitations of imaging. On the other hand, asymmetries in the cartilage should alert the radiologist to scrutinize the adjacent laryngeal soft tissues for signs of tumor infiltration (Figs. 206.1 and 206.4).

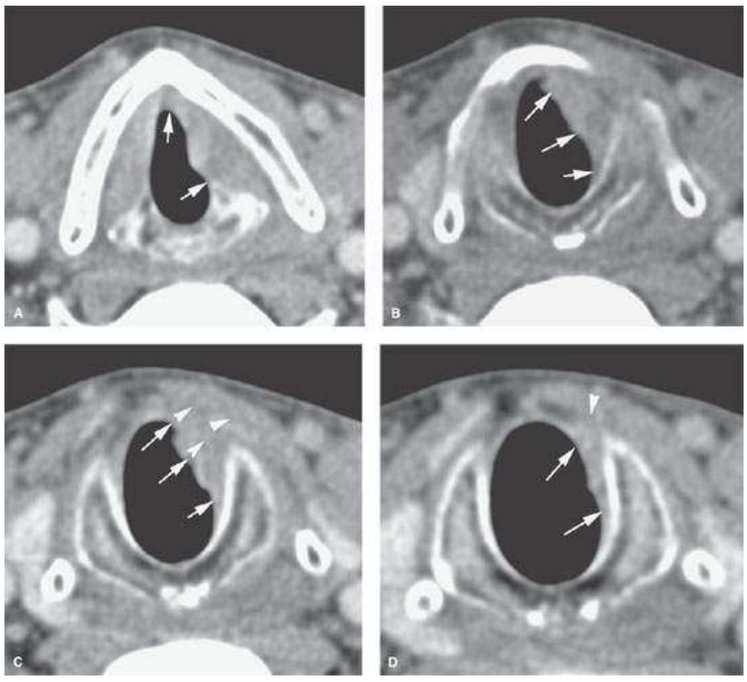


FIGURE 206.3. A patient presenting with what was believed to be true vocal cord paralysis. Computed tomography study from the posterior fossa to the aortopulmonary window showed no abnormality along the vagus or recurrent laryngeal nerves. It did, however, show an infiltrating tumor of the larynx that was entirely submucosal. A: The tumor involves the entire true cord up to the anterior commissure (arrows). B: Subglottic spread is present (arrows). C: The subglottic spread (arrows) extends through the cricothyroid membrane into the soft tissues beneath the infrahyoid strap muscles (arrowheads). D: Continued subglottic spread is present almost to the bottom of the cricoid cartilage (arrows).

Early cartilage invasion is best assessed by a combined commonsense and objective consideration of factors that can assign risk of invasion and relate it to treatment outcome. In taking such a risk-profiling approach, cartilage invasion may be only one of several factors influencing outcome. Some basic factors about the primary tumor can help to assess early cartilage invasion. These include site of origin and volume of the primary tumor; known proclivity of primary tumors at that site relative to cartilage invasion; infiltrating versus pushing tumor margins; degree of cartilage ossification adjacent to tumor; whether cartilage ossification is symmetric; sclerosis of cartilage adjacent to tumor; focal or diffuse obliteration of the fatty marrow space; possible invasion of connecting membranes connecting cartilages; and edema of extralaryngeal soft tissues manifesting, in early cases, as loss of the fat plane between the infrahyoid strap muscles and the cartilage if such a plane is present in the patient.

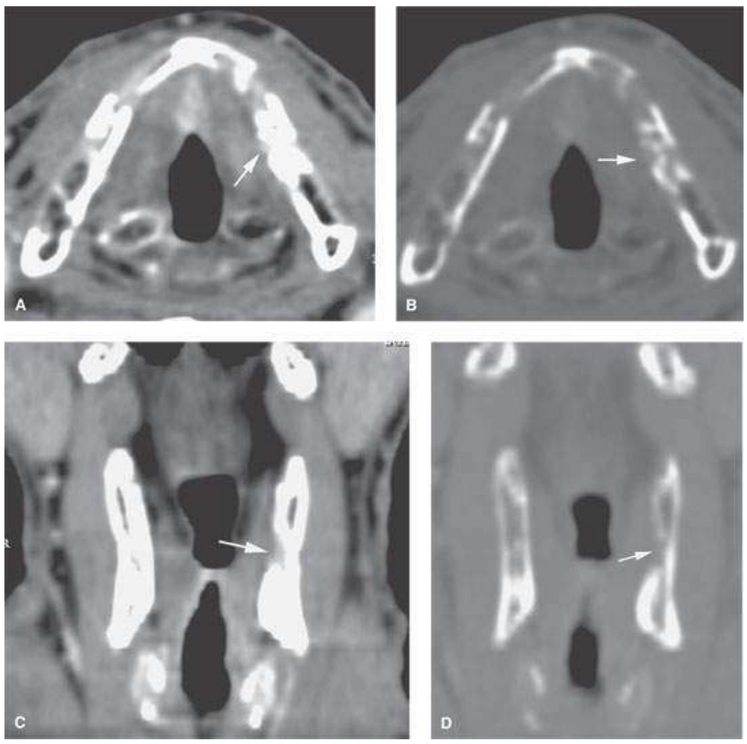


FIGURE 206.4. A patient with an early transglottic tumor and computed tomography (CT) demonstrating probable focal thyroid cartilage invasion. The case also illustrates the excellent quality reformations that are currently available with multidetector CT. A: Tumor of the true cord thickens the anterior commissure and obliterates the paraglottic fat at a level just above the laryngeal ventricle (arrow). B: Bone window settings show the focal defect in the thyroid cartilage more clearly suggesting very early cartilage invasion (arrow). C, D: Coronal reformations confirm the presence of a defect in the low paraglottic space along the inner margin of the thyroid lamina (arrows). Such defects can be normal variants; they might also represent early cartilage invasion. (NOTE: The significance of very minimal cartilage invasion with regard to an impact on survival is uncertain and at this time doubtful. Refer also to Fig. 206.5 for correlating information.)

Cartilage invasion has, for years, been a putative marker for a tumor at an increased risk of failing radiotherapy (RT). This belief was justifiable in the pre-CT era when detection of cartilage invasion depended on palpation and plain film evidence of cartilage erosion. By the time that cartilage invasion was detected using these now primitive diagnostic tools, however, the patient was clearly beyond cure with RT. The detection of early cartilage invasion by CT and MR provides more accurate tumor staging information and can be used to determine the best treatment modality. Cartilage invasion or an increased risk of cartilage invasion should be part of a risk profile in selecting the strategy for cure, preserving as much laryngeal function as possible.2

Subtle macroinvasion may be evaluated as described previously in this discussion; however, there will always be false-positive and -negative studies in this regard. Risk of micro- or macroinvasion can be assessed by simple imaging parameters. The concept was first introduced by Archer et al.3 using tumor axial dimensions and positions. Such a risk profile for micro- or early macroinvasion can be even more productively linked to a predictive model for treatment outcome. This method relies only on generating a tumor volume and observing whether the cricoid, arytenoids, and/or thyroid cartilages adjacent to tumor are

sclerotic. This method can stratify patients with T3 glottic cancers into high, medium, and low risk of failure with RT alone.4 Although the risk of failure may be related to laryngeal framework invasion, its prognostic impact has not been proven (Figs. 21.44, 206.4, and 206.5).

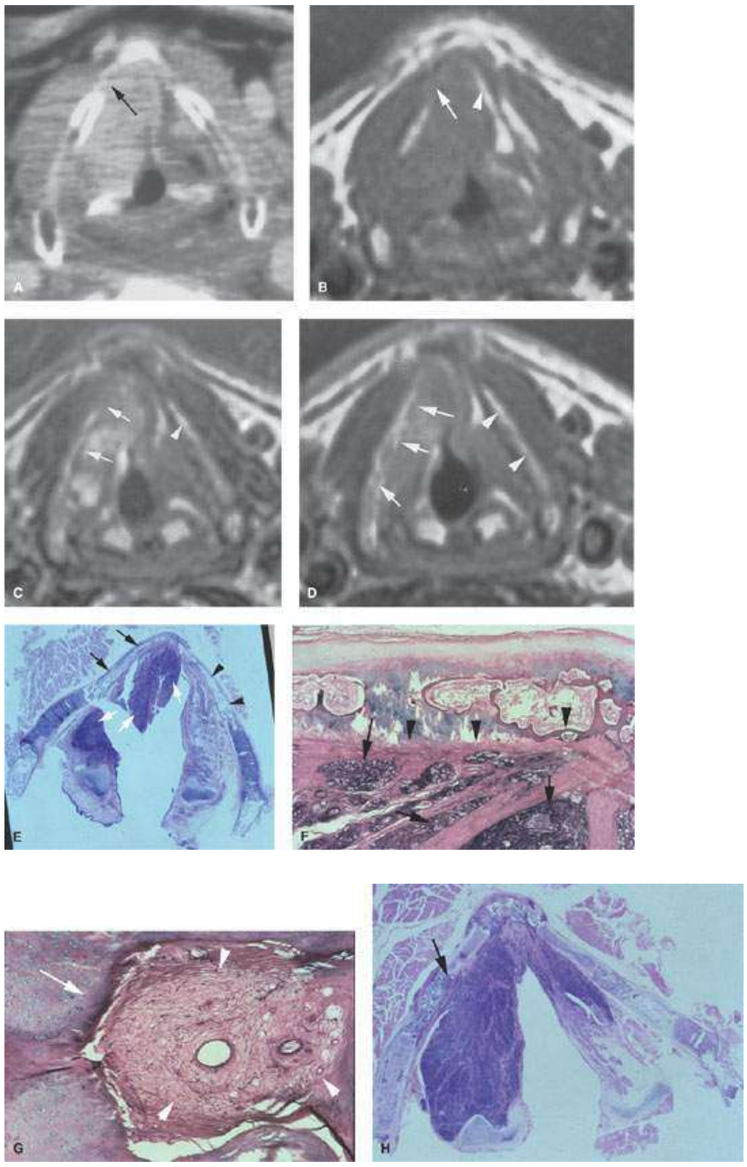


FIGURE 206.5. Patient with false vocal cord carcinoma. A: Computed tomography showing possible thyroid cartilage invasion (arrow). B: The non–contrast-enhanced T1-weighted (T1W) image again is suspicious for invasion with possible obliteration of fat within the thyroid cartilage (arrow) compared to the fat within the thyroid lamina on the normal side (arrowhead). C: Contrast-enhanced T1W image showing irregularity and enhancement along the thyroid lamina suspicious for invasion compared to the appearance of the lamina on the normal side (arrowheads). D: A T2-weighted image again suggests infiltration of the marrow space of the thyroid lamina (arrows) compared to the normal side (arrowhead). E: Whole organ section on this patient through the false cord level. Tumor (white arrows) is present in the soft tissues; however, the thyroid cartilage is not invaded. The thyroid lamina on the right (arrows) is not as well ossified as on the left (arrowheads), where it is obviously ossified and contains a fatty marrow space. F: Close-up photomicrograph showing no evidence of tumor invading the perichondrium interface with the thyroid lamina either at cartilaginous portions of the thyroid lamina or at ossified portions (arrowheads). Tumor obviously infiltrates the deep soft tissues (arrows). G: Multiple areas of fibrosis (arrowheads) were found within the cartilage of the right thyroid lamina. Such reactive changes are sometimes incited by adjacent tumor and mimic cartilage invasion. This patient could likely have been controlled by radiotherapy rather than laryngectomy based on these findings. H: Photomicrograph of a whole organ section of Patient 3 showing a small area of cartilage invasion (arrows) similar to that seen in Figure 206.4. It is uncertain whether recognizing such minimal areas of cartilage invasion are a benefit or a detriment to strategies that aim to conserve laryngeal function while improving survival in patients with laryngeal carcinoma. (Material in this figure courtesy of Minerva Becker, M.D., Geneva, Switzerland.)

CT and MRI easily identify tumor growing outside of the larynx, usually via the thyrohyoid and cricothyroid membranes/ligaments to the soft tissues of the neck. Such spread is normally easy to distinguish from cervical lymph nodes metastases. Spread to the thyroid gland, pharynx, and cervical esophageal verge is also assessed.

FDG-PET for Staging

In most laryngeal neoplasms, FDG-PET has a modest, if any, primary role to play (Fig. 206.2D–H), as this technique does not allow one to reliably assess the anatomic extent of the lesion and the possible invasion of the tumor into adjacent structures. Its value in determining or planning gross tumor volume for RT planning is controversial, especially in smaller laryngeal cancers.

FDG-PET can detect neck nodal metastasis with relatively high accuracy, but both false-positive and false-negative results occur. Although FDG-PET sometimes detects nodal metastasis missed by other imaging techniques, the high cost of this technique does not warrant its routine use for this indication. It is certainly not an appropriate routine study in patients with T1 and T2 glottic cancers.

It may be warranted in other circumstances in the patient population with these cancers to detect distant metastases and coincident primary tumors outside the head and neck region. This technique must be used selectively rather than applied indiscriminately for diagnosis and staging given its expense and often low potential to truly alter management or outcome.

In advanced laryngeal cancer (T4) or in patients with adenopathy low in the neck (levels 4, 5B, or 6), adding an FDG-PET study may be useful to exclude distant metastasis. In tumors requiring very extensive resections, FDG-PET is also useful to exclude a second primary tumor to avoid unnecessary mutilation of the patient.

In the posttreatment situation, FDG-PET may sometimes be helpful as discussed in a following section surveillance options.

Tumor response to chemotherapy as measured by FDG-PET is being investigated as a way to select patients who would benefit from chemoradiation organ preservation therapy versus surgery and postoperative RT treatment strategies. This application is not yet proven to be beneficial, as discussed in Chapter 21 (Fig. 21.63). Tumor perfusion may eventually be a better parameter in this regard.

SPECIFIC DISEASE/CONDITION

Laryngeal Squamous Cell and Other Carcinomas

Etiology

SCCA of the larynx is clearly linked to cigarette smoking. Alcohol is a contributing and likely potentiating risk factor but probably less so than in cancer in other head and neck sites. No other etiologies have been proven. Other carcinomas are of predominantly glandular origin and are sporadic and not necessarily linked to known predisposing factors.

Prevalence and Epidemiology

Laryngeal carcinoma is a common disease in the smoking population. There is about 10:1 male to female predominance.5 Localized and regional disease accounts for the vast majority of cases at presentation, with distant metastasis being uncommon of patients at the time of initial diagnosis. Glottic cancer is more prevalent than supraglottic cancer. The rates of occurrence are increasing in both males and females but proportionally much more in females.

Clinical Presentation

TVC cancer produces hoarseness as the initial symptom. Sore throat, ear pain, pain localized to the thyroid cartilage, and airway obstruction may occur in advanced lesions. Glottic and subglottic cancers occasionally present with stridor or airway symptoms.

Hoarseness is usually not a presenting symptom in patients with supraglottic cancer but may occur in the presence of advanced disease. Changes in voice quality do occur. Dysphagia and referred otalgia (from the vagus to the Arnold nerve) are common presenting complaints. In supraglottic cancer, a neck mass due to metastatic adenopathy is a common presenting sign.

Physical examination is mainly done by rigid and flexible fiber-optic endoscopes. The physical examination should establish whether the vocal cord is mobile, paretic, or fixed.

Ulceration of the infrahyoid epiglottis and/fullness of the vallecula may indicate pre-epiglottic space invasion. Fullness to palpation of the thyrohyoid membrane region may also suggest invasion of the pre-epiglottic space.

The laryngeal click, which can be elicited by media to lateral manual manipulation of the larynx over the vertebral column, may become absent in the presence of postcricoid spread.

Localized pain or tenderness to palpation over the lamina suggests gross invasion of the cartilage.

Pathology

The laryngeal surfaces of the epiglottis and TVCs are lined with stratified squamous epithelium. Otherwise, the larynx is lined with pseudostratified ciliated columnar epithelium. This squamous cell surface epithelium is the source of nearly all squamous laryngeal malignancies. Benign and malignant minor salivary gland tumors arise from the mucous glands deep to the laryngeal mucosa.

Most of the vocal cord carcinomas are either well differentiated or moderately well differentiated. Sometimes there is an apparent carcinoma and sarcomas occurring together, but these tumors are usually squamous carcinomas with a pseudosarcomatous or spindle cell stromal reaction. Spindle cell carcinomas in the larynx and trachea may present as polypoid or pedunculated masses that have a very favorable prognosis. Verrucous carcinoma occurs in a very small percentage of patients, but histologic diagnosis is difficult and must correlate with the gross appearance of the lesion. Supraglottic carcinomas tend to be less differentiated than TVC primaries. Small cell carcinoma (Fig. 30.14) is rarely diagnosed in the supraglottic larynx. It is biologically very aggressive with a high risk for distant spread.

General Common Pathways and Trends

Generally, tumor growth in the larynx is directed by existing natural anatomic barriers. A tumor margin may be infiltrative or have pushing, well-defined borders as discussed in Chapter 21. There is a tendency for supraglottic and glottic lesions to remain, at least for a time, confined to their compartments of origin. However, there is no real anatomic barrier that restricts spread from one area to the next.

Glottic cancers tend to be slow growing but may extend to the supraglottis and subglottis over time. Because supraglottic cancers often arise well above the TVC, TVC involvement is usually a late phenomenon. Supraglottic cancer may spread to the TVC level via the paraglottic space deep to the FVC and laryngeal ventricle mucosa. The fibrous ligament at the anterior commissure is a relative barrier to midline submucosal tumor spread from the epiglottis to and below the anterior commissure; thus, involvement is mainly a surface phenomenon as seen in the anterior, inferior spread of supraglottic cancers.

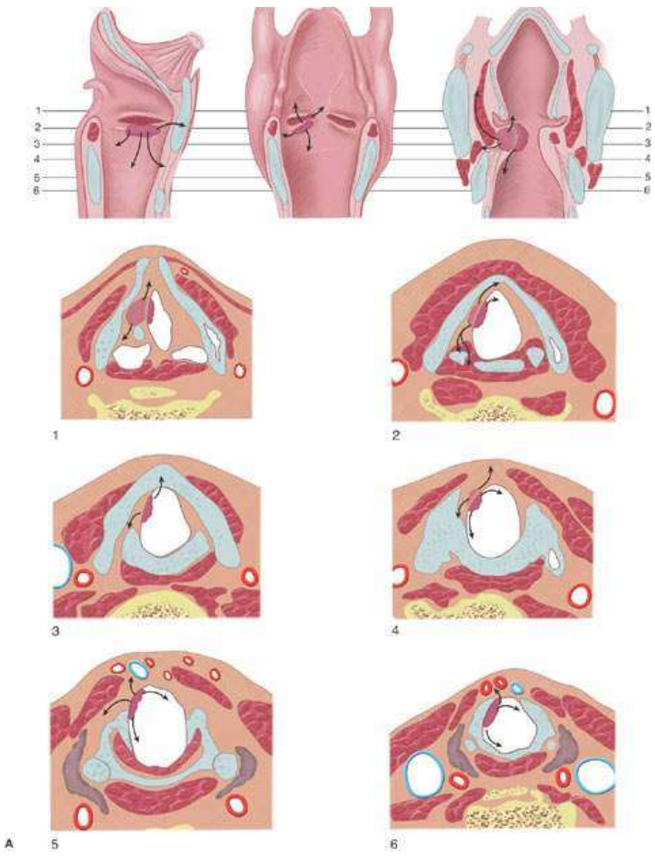
The pre-epiglottic and paraglottic spaces are predominantly fatty. The quadrangular membrane may have a minor role in directing submucosal tumor spread for infrahyoid epiglottic, FVC, and TVC lesions (Fig. 206.6A–C). As the FVC and TVC tumors spread laterally, they reach the thyroid cartilage and are most often deflected growing superiorly and inferiorly within the paraglottic space (Fig. 206.7). Sometimes the cancer grows through the cricothyroid and thyrohyoid membranes before invading the thyroid lamina (Fig. 206.8). Tumor headed inferiorly within the paraglottic space is commonly diverted by the conus elasticus (Figs. 201.3–201.8). Tumor often grows toward and then through the cricothyroid membrane and into the tissues of the neck, where it may invade the thyroid gland. Such spread beyond the laryngeal skeleton is most often contained by the infrahyoid strap muscles. In advanced cases, tumor may grow across the visceral compartment fascia to invade the superficial fascia and eventually the subcutaneous fat and skin.

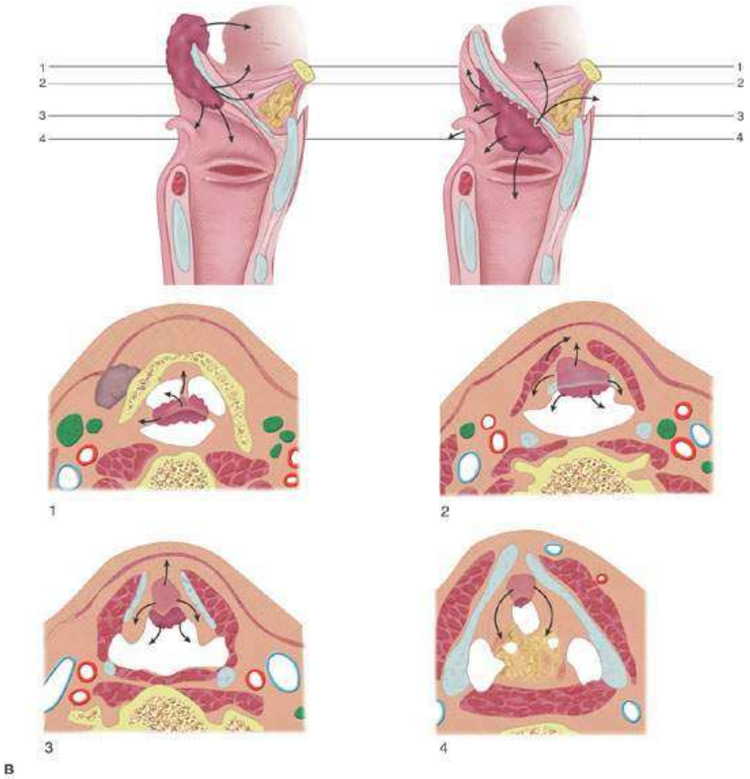
Thyroid cartilage invasion usually begins in an ossified section of the cartilage (Figs. 206.4 and 206.5). The specific access for invasion of the ossified cartilage is often along areas where there are small fissures, created by penetrating ligaments and connecting membranes and neurovascular bundles. This likely explains why glottic cancer involving the anterior commissure invades the thyroid cartilage at the point of attachment of the vocal ligament (Fig. 206.9). Cancer spread directed inferiorly by the conus elasticus and cricothyroid membrane will invade their attachments along the upper margin of the cricoid and lower margin of the thyroid cartilage. Supraglottic cancers only infrequently invade the adjacent thyroid lamina. Such invasion is usually at the insertion of the thyrohyoid membrane along the upper margin of the thyroid lamina. Tumor spreading in the paraglottic space often has a broad zone of contact with the perichondrium of the thyroid cartilage (Fig. 206.10). However, direct invasion of the adjacent lamina away from its edges and sites of membrane and muscle insertions is uncommon and almost assuredly is due to invasion along vessels penetrating the ossified portion of the thyroid lamina.

Micheau et al.6 studied 120 cases of T2 through T4 laryngeal cancers without preoperative radiation. In the 70 patients with cartilage invasion, 66 patients had invasion that occurred at the ossified sites. The authors noted that the most common site of thyroid cartilage invasion occurs at the anterior angle and that apparently discontinuous spread within the marrow space of an ossified thyroid lamina occurs.

Archer et al.,3 in the early days of laryngeal CT, showed that when the average diameter of the tumor mass was .16 mm and the lesion center was located below the superior process of the arytenoid cartilage, 12 of 14 patients had cartilage invasion on pathologic examination. Nine of the 12 had three cartilages

invaded. Cartilage invasion could only be detected by microscopic examination in 8 patients. This experience presaged the concept developed about 5 to 10 years later that tumor volume combined with arytenoid, thyroid, and/or cricoid cartilage sclerosis is a reasonable way to predict microscopic cartilage invasion, with the surrogate outcome for likely cartilage invasion in these later studies being risk of RT failure in T3 glottic cancers. This was first suggested by Lee et al.[7] and then refined by Pameijer et al.[4] Imaging-based risk stratification has shown that fixed-cord T3 glottic cancer with volume, 3.5 cc and no cartilage sclerosis could be controlled by RT alone in .90% of cases. Those with tumor volume of $3.5 cc and sclerotic changes of one of the three cartilages had a 40% to 60% chance of control with RT alone. If tumor volume was .3.5 cc and two or three cartilages were sclerotic, there was a 90% risk of failure with RT alone. A separate investigation[8] of cricoid cartilage abnormalities in glottic carcinoma yielded a statistically significant lower control rate after RT. Ten out of the 13 patients with sclerosis of the cricoid in this study also had sclerosis of the arytenoid cartilage, corresponding with the "double sclerosis" situation (arytenoid and cricoid cartilage involvement) described by Pameijer et al.[4] However, when multivariate analysis was performed, cartilage abnormalities were no longer predictive of failure when paraglottic and pre-epiglottic space involvement were included in the analysis. Even relatively subtle cartilage abnormalities are often correlated with deep tumor extension. Deep involvement of the paraglottic space at the glottic level, as seen on imaging studies, is also referred to as the "adjacent sign" due to tumor growing adjacent to the thyroid cartilage. This sign was found to be the only independent predictor of local outcome and survival in a series of 130 patients with T1 and T2 glottic cancer.[9] It appears that cartilage abnormalities are an epiphenomenon of large tumor volume and deep tumor extension, which are probably better predictors of local outcome after RT.





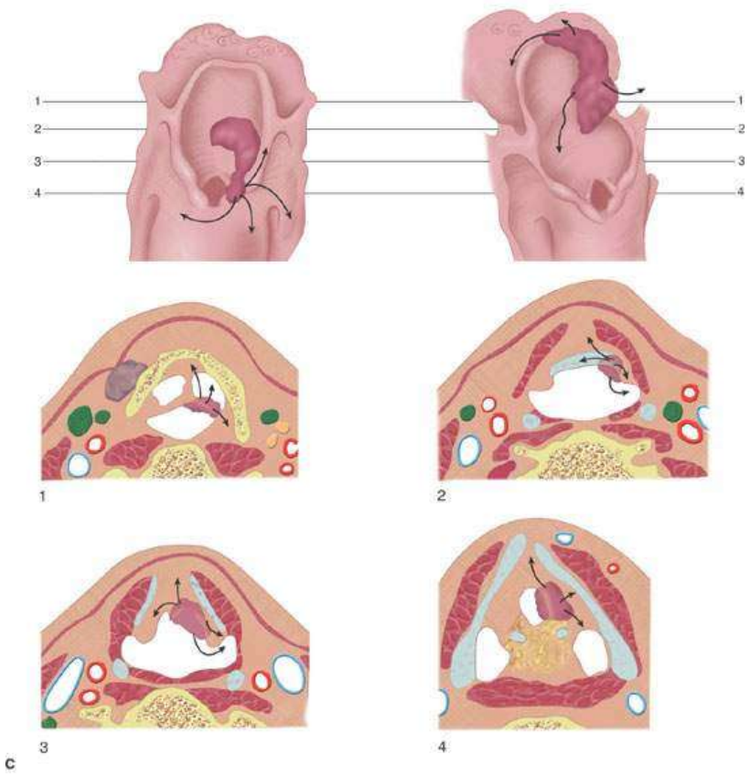


FIGURE 206.6. Spread patterns of laryngeal cancer. A: Glottic carcinoma spread patterns. B: Spread patterns of epiglottic cancer both of the infrahyoid and suprahyoid epiglottis. C: Spread patterns of marginal supraglottic lesions including those of the aryepiglottic fold, false cord, and laryngeal ventricle mucosa.

Other evidence of deep tumor invasion is fixation of the vocal cord. This is usually caused by invasion or destruction of the vocal muscles, invasion of the cricoarytenoid joint, or rarely invasion of the recurrent laryngeal nerve. Perineural spread is uncommon in laryngeal malignancies.

Supraglottis

Supraglottic cancers are often epiglottic in origin. However, it might be difficult to precisely tell the subsite of supraglottic origin of advanced lesions except by its appearance on CT or MR images. Even with those tools, it is sometimes difficult.

Suprahyoid Epiglottis

Lesions of the suprahyoid epiglottis (Fig. 206.6B,C) may appear predominantly as an exophytic mass with little inclination to destroy the epiglottic cartilage or spread to adjacent structures or deep spaces. Some may infiltrate the free margin of the epiglottis, destroying the cartilage and amputating its tip. These latter cancers tend to invade the mucosa of the vallecula and lateral pharyngeal walls (Fig. 206.11). To some extent, the predominantly superficial or deep spread of epiglottic cancer may be directed by the quadrangular membrane, which is a relatively weak barrier to tumor spread.

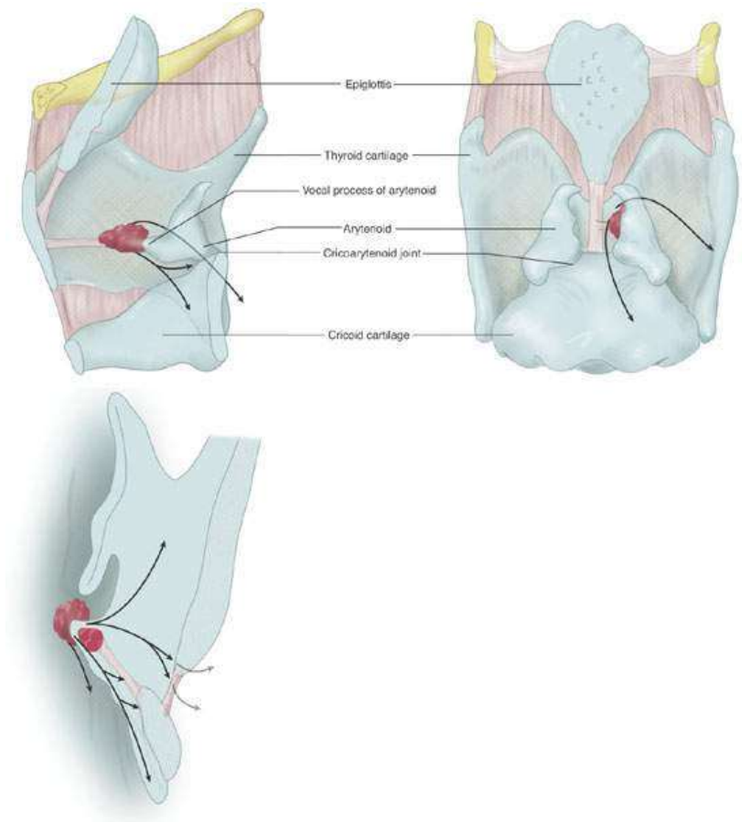


FIGURE 206.7. Spread patterns of glottic carcinoma, especially with regard to threats to the cricoid and arytenoid cartilages and occult patterns of deep spread within the paraglottic space.

Infrahyoid Epiglottis

Lesions of the infrahyoid epiglottis (Fig. 206.6B,C) produce irregular nodular mucosal masses often showing simultaneous invasion through the porous epiglottic cartilage and thyroepiglottic ligament into the pre-epiglottic space (Fig. 206.12). Tumor may spread superiorly within the pre-epiglottic space and involve the vallecula and base of the tongue without involving the suprahyoid epiglottis or showing any other clinically obvious mucosal contiguity (Fig. 206.13).

Cancers of the infrahyoid epiglottis also grow circumferentially to involve the aryepiglottic folds and thereby the medial wall of the pyriform sinus. Inferolateral growth will eventually reach the false vocal folds, and superolateral growth will extend to the pharyngoepiglottic fold. Invasion of the anterior commissure and TVCs is usually a late occurrence, and subglottic extension occurs occasionally in similarly advanced lesions. Such "transglottic" growth is much more typical of FVC cord and ventricular primaries. Infrahyoid epiglottic lesions that grow in a transglottic manner are at high risk for thyroid cartilage invasion, even if the vocal cords are mobile.

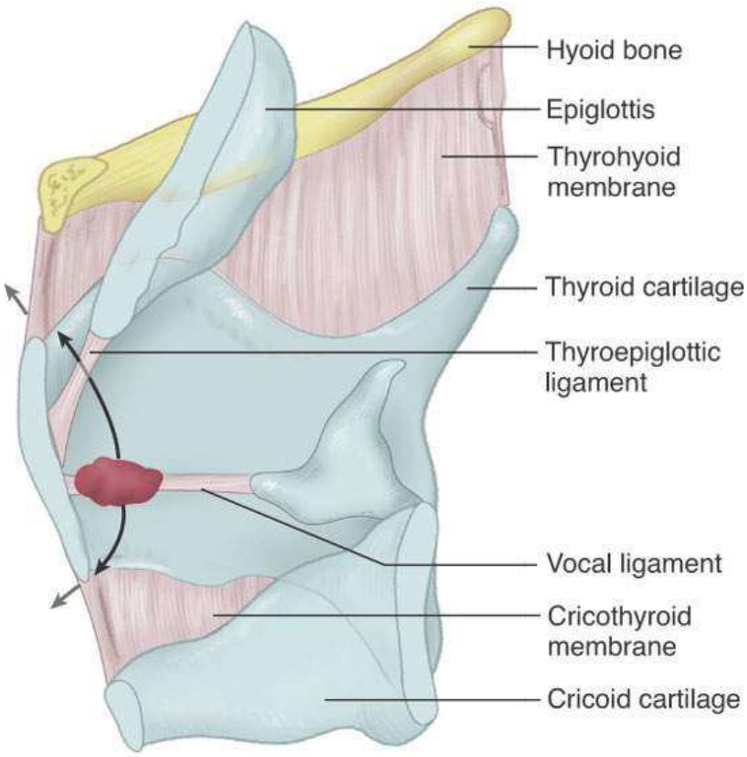


FIGURE 206.8. Patterns of spread of cancers arising at or near the anterior commissure and in particular their tendency to spread early to involve the laryngeal skeleton.

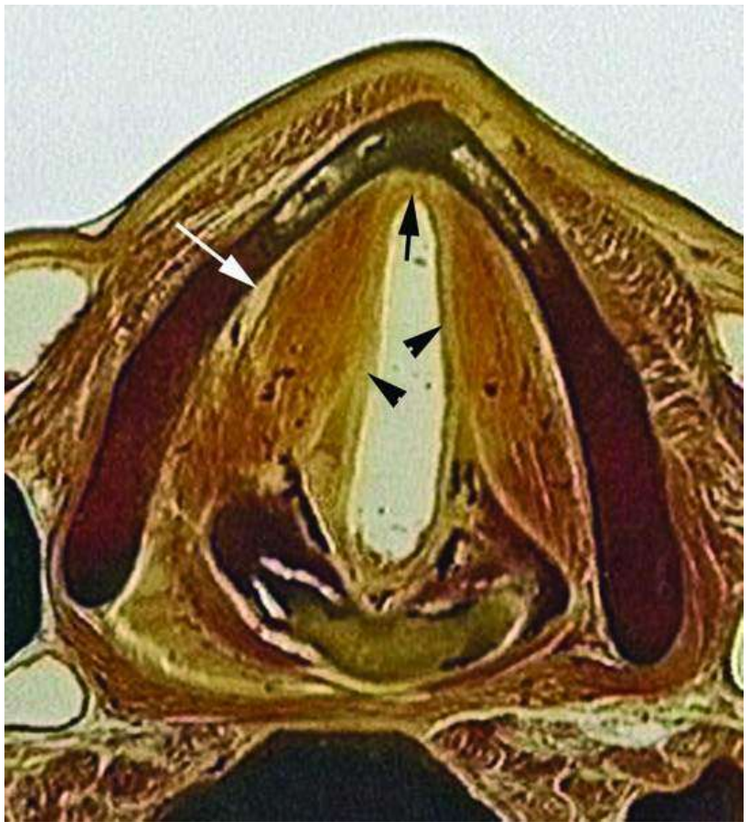


FIGURE 206.9. Whole organ section demonstrating the relationship of the vocal ligaments (arrowheads) to the anterior commissure insertion of the vocal ligaments (arrow). It also demonstrates the fatty paraglottic space (white arrow) between the muscles of the true cord and the thyroid lamina.

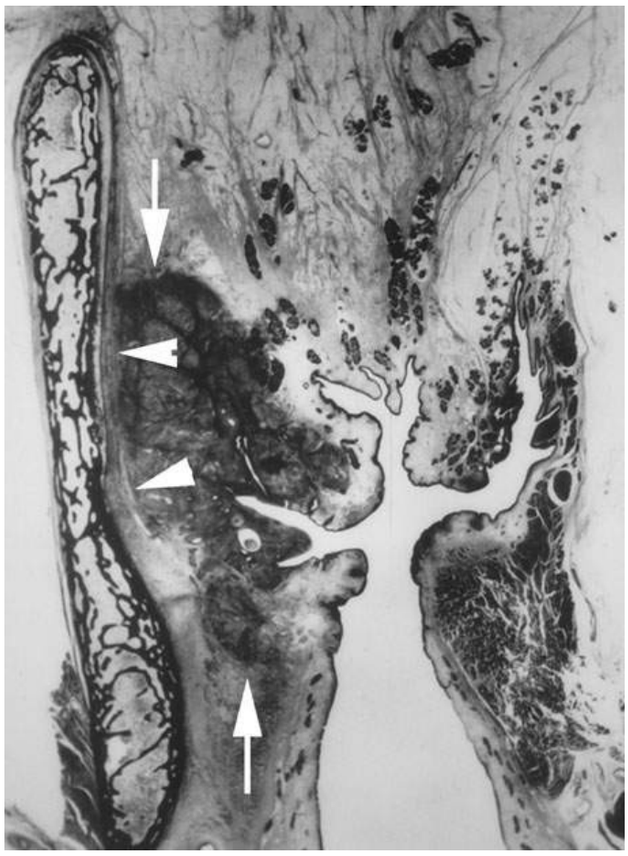


FIGURE 206.10. Coronal whole organ section showing a transglottic cancer spreading from the upper subglottis superiorly to the mid supraglottis (arrows). There is extensive tumor in the paraglottic space, but it does not invade the thyroid lamina (arrowheads).

False Vocal Cord/Ventricle

FVC carcinomas (Figs. 206.6C and 206.7) are usually infiltrative, ulcerative, and endophytic. These cancers invade the paraglottic space early in development and may often spread a considerable distance beneath intact mucosa without producing physical signs (Figs. 6.3, 206.14, and 206.15). This growth pattern leads to understaging at physical examination. These tumors frequently have a broad zone of contact with the perichondrium of the thyroid cartilage early on, but cartilage invasion is a late phenomenon. Spread medially to the lower portion of the infrahyoid epiglottis with invasion of the pre-epiglottic space is uncommon. Paraglottic space submucosal extension to involve the vocal cord can occur, and such vocal cord invasion is often associated with thyroid cartilage invasion. Submucosal extension to the anterior and medial walls of the pyriform sinus occurs early. Subglottic extension occurs only in advanced lesions.

Aryepiglottic Fold/Arytenoid

Early lesions in aryepiglottic fold/arytenoid (Figs. 206.6C and 206.14) may be entirely exophytic. As the lesions enlarge, they invade the cricoarytenoid joint and eventually cause fixation of the TVC. Advanced lesions grow in the paraglottic space to invade the thyroid, epiglottic, and cricoid cartilages (Figs. 206.16 and 206.17). Eventual spread to the base of the tongue and pharyngeal wall may occur via these submucosal pathways. Since the medial wall of the pyriform sinus and aryepiglottic fold are essentially common structures, it may be difficult to determine where the lesion started. Spread to the pyriform sinus apex identifies it as a pyriform sinus cancer. Spread to the remaining supraglottis superiorly and fat in the aryepiglottic fold suggests a marginal supraglottic (aryepiglottic fold) primary.

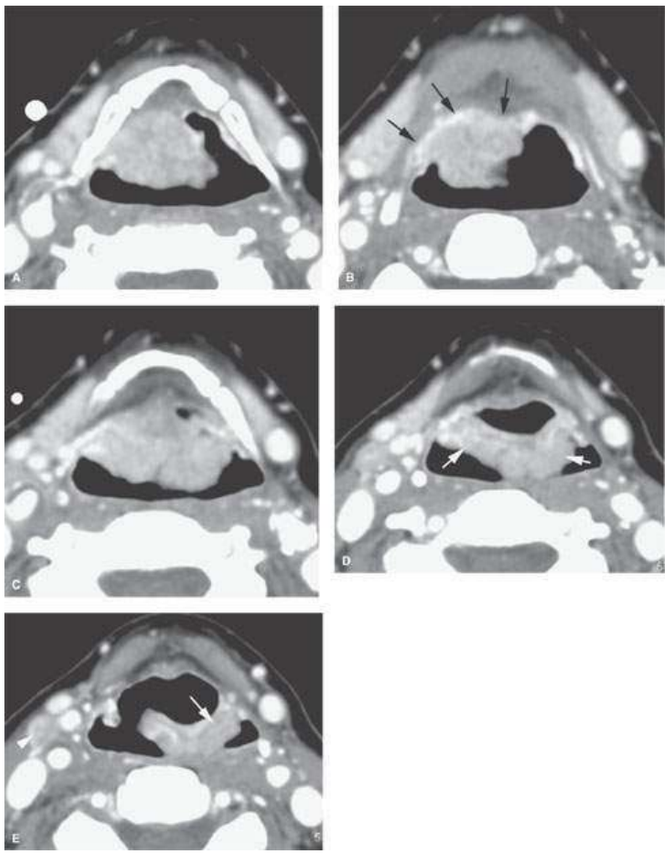
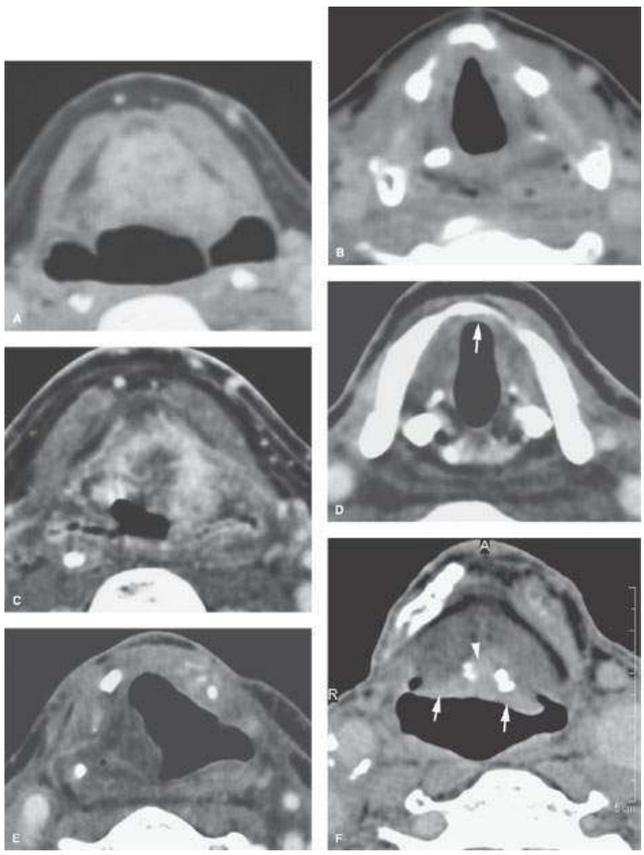


FIGURE 206.11. Contrast-enhanced computed tomography scan of a patient with cancer of the suprahyoid epiglottis. A: This bulky exophytic lesion encompasses the suprahyoid epiglottis. B: The tumor spills superiorly from (A) into vallecula to involve but not invade the tongue base mucosa (arrows). C: Tumor extends to the base of the suprahyoid epiglottis in an exophytic plaquelike manner. D: Tumor continues inferiorly along the pharyngoepiglottic folds and upper aryepiglottic folds and in (E) continues inferiorly along the aryepiglottic fold (arrow).



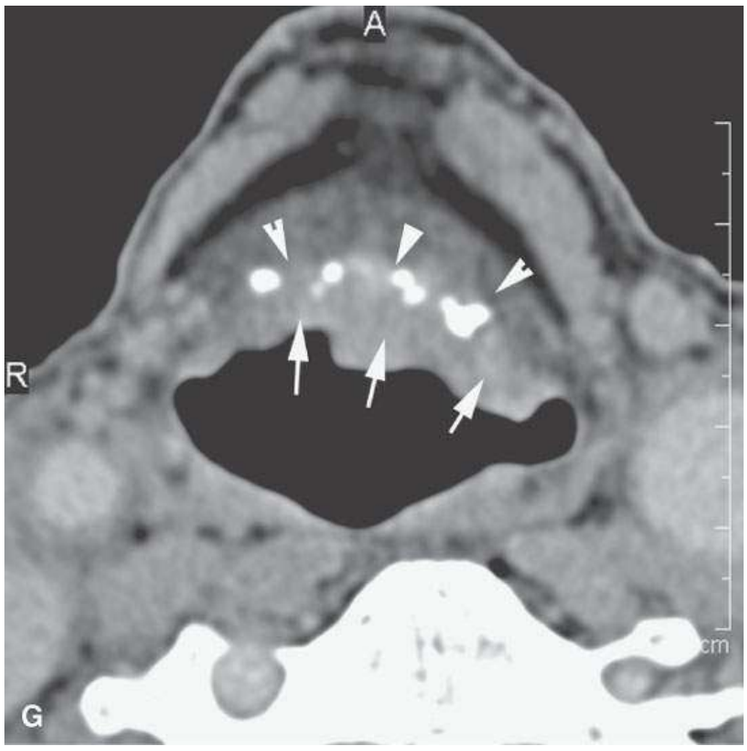


FIGURE 206.12. Two patients with carcinomas of the infrahyoid epiglotis A–E: Contrast-enhanced computed tomography (CECT) study in Patient 1 with deeply infiltrating carcinoma of the infrahyoid epiglottis. In (A), the tumor is endophytic nearly entirely and filling the pre-epiglottic space. In (B), the tumor ended well above the anterior commissure, and the patient was suitable for supraglottic laryngectomy. In (C), the patient elected radiotherapy (RT). A baseline study done about 3 months after the completion of RT showed little response of the tumor (C). In (D), the persistent tumor still ended well above the anterior commissure, so the patient was suitable for supraglottic laryngectomy. In (E), the patient status post supraglottic laryngectomy shows gross total resection. The patient was cured. F, G: CECT study of Patient 2 with an exophytic plaquelike lesion of the infrahyoid epiglottis to contrast with the lesion in (A) through (E). In (F) and (G), at the junction of the infrahyoid and suprahyoid epiglottis, there is plaquelike tumor along the laryngeal surface (arrow). There is minimal invasion of the pre-epiglottic space through the calcified epiglottic cartilage (arrowhead). G: Somewhat more inferiorly the tumor spread along the infrahyoid epiglottis is mainly exophytic. There is no significant penetration of tumor through the calcified epiglottic cartilage into the preepiglottic space (arrowheads). (Note: This second cancer was very suitable for supraglottic laryngectomy or radiation cure. The patient had severe lung disease and was radiated and cured.)

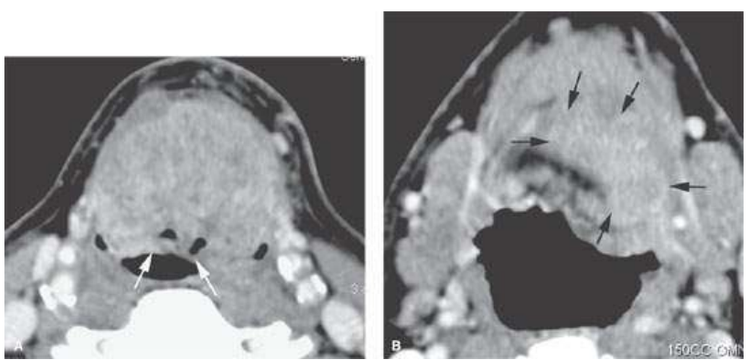


FIGURE 206.13. Contrast-enhanced computed tomography in a patient with supraglottic carcinoma. A: Very extensive spread from the pre-epiglottic space into the tongue base. This was all submucosal. The relatively normal suprahyoid epiglottis is still visible (arrows). B: This tumor continued cephalad well into the tongue base, showing a very aggressive infiltrating pattern along the left lingual neurovascular bundle crossing the midline (arrows).

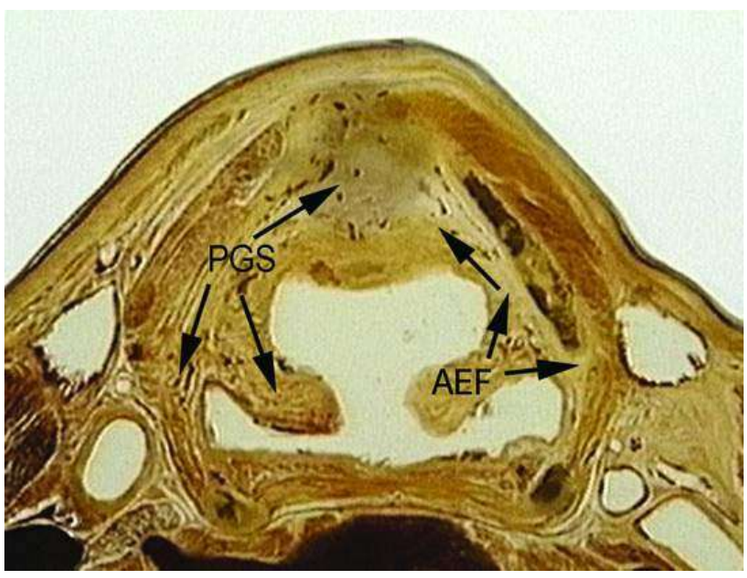


FIGURE 206.14. Whole organ anatomic section demonstrating potential routes of spread of tumor from the paraglottic space (PGS) and aryepiglottic fold (AEF) to surrounding structures, including the pre-epiglottic space and laryngeal skeleton as well as the adjacent pyriform sinus (arrows). These are typical spread patterns of marginal epiglottic lesions.

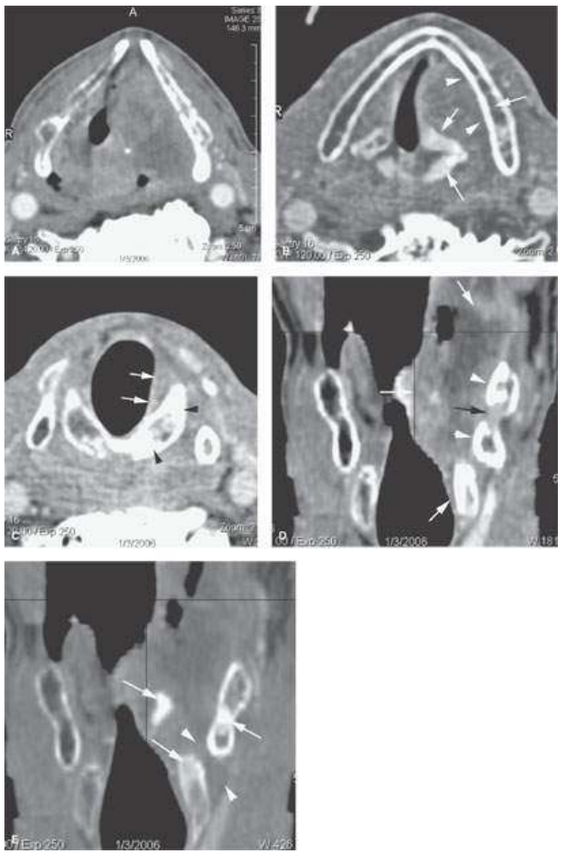


FIGURE 206.15. Contrast-enhanced computed tomography study of a patient with a false cord carcinoma that grew across the true cord. A: Very bulky endophytic tumor is present at the false cord level. B: At the true cord level, the tumor spreads within the paraglottic space (arrowheads) widening the space between the cricoid cartilage and thyroid lamina. Note the reactive sclerosis of the arytenoid cartilage, top of the cricoid cartilage, and thyroid lamina (arrows) compared to those structures on the normal side. Tumor adjacent to cartilage frequently incites reactive osteitis without actually invading cartilage. Such reactive sclerosis also may account for the increased density within the thyroid cartilage marrow space. This can be due to fibrosis as well. Refer also to Figure 206.5. C: Tumor continues inferiorly within the subglottic space (arrows). The cricoid cartilage is sclerotic due to surrounding tumor (arrowheads), as is the inferior cornu of the thyroid cartilage with loss of the fatty appearance of its marrow space. D: Coronal reformatted image showing the extensive transglottic tumor spreading from the upper paraglottic space to the low subglottic space (white arrows). There is an area strongly suggestive of invasion of the thyroid lamina (black arrow) and a broad zone of tumor within the paraglottic space adjacent to the thyroid lamina (white arrow). E: Bone windows of a coronal reformatted image showing tumor growing between the thyroid lamina and cricoid cartilage (arrowheads) into the neck. This demonstrates sclerosis of all three cartilages (arrows) compared to the normal side. There was only minimal cartilage invasion in the laryngectomy specimen.

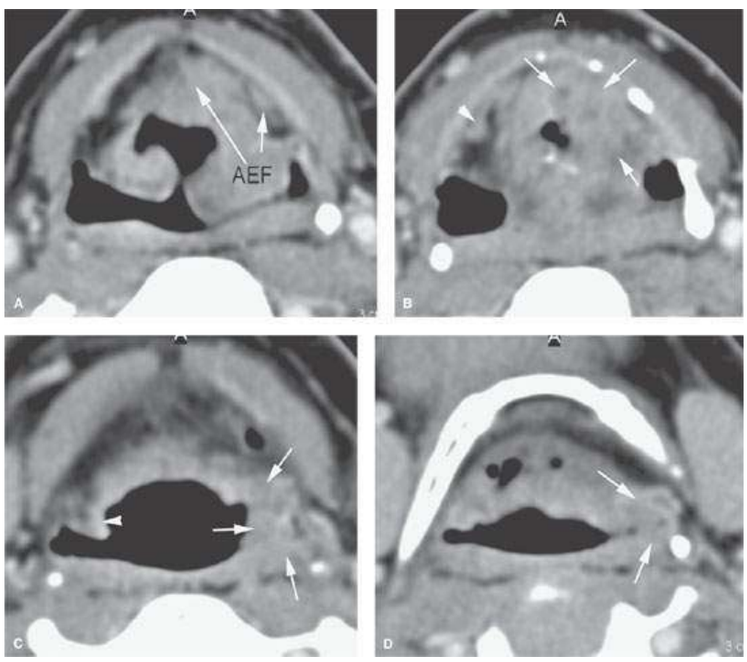


FIGURE 206.16. Typical relatively low volume marginal supraglottic lesion as seen on contrast-enhanced computed tomography. A: This is a primary lesion of the aryepiglottic fold (AEF) spreading from the fold to the pre-epiglottic space and paraglottic space (arrows). B: A section inferior to that seen in (A) showing widespread infiltration of the paraglottic space and low pre-epiglottic space (arrows) compared to the normal side (arrowhead). C: More superior sections showing tumor spreading up the aryepiglottic fold (arrows), thickening the fold compared to the normal side (arrowhead). D: Relatively low volume exophytic tumor spreading superiorly to the junction of the aryepiglottic fold and pharyngoepiglottic fold (arrows). (NOTE: This was a relatively low volume supraglottic carcinoma, being just under 6 cc. It was successfully treated with radiotherapy.)

Vocal Cord

Most vocal cord cancers begin on the free margin and upper surface of the TVC. About two thirds are confined to the TVC level at initial diagnosis (Figs. 206.6A and 206.7–206.9). The anterior third of the TVC is the most common site of origin, and extension to the anterior commissure is common (Fig. 206.3). Isolated anterior commissure cancers account for very few of all TVC cancers (Fig. 206.18).

Tumors at the anterior commissure may extend along the short anterior commissure tendon that attaches directly into the thyroid cartilage, so the cancer grows into the thyroid cartilage without having to grow through the perichondrium. Anterior commissure invasion frequently leads to early anterior subglottic spread,

and from there tumor may then grow through the cricothyroid membrane into the prelaryngeal soft tissues (Figs. 206.19 and 206.20).

Cancers starting on the posterior half of the TVC are more likely to grow along the submucosa onto the medial surface of the arytenoid vocal process (Figs. 206.6A and 206.7). From there, the cricoarytenoid joint and interarytenoid areas are frequently invaded. Such extension may be difficult to appreciate endoscopically, which can result in understaging of more posterior TVC cancers. These tumors may spread anteriorly beneath the mucosa within the Reinke space (Fig. 206.3).

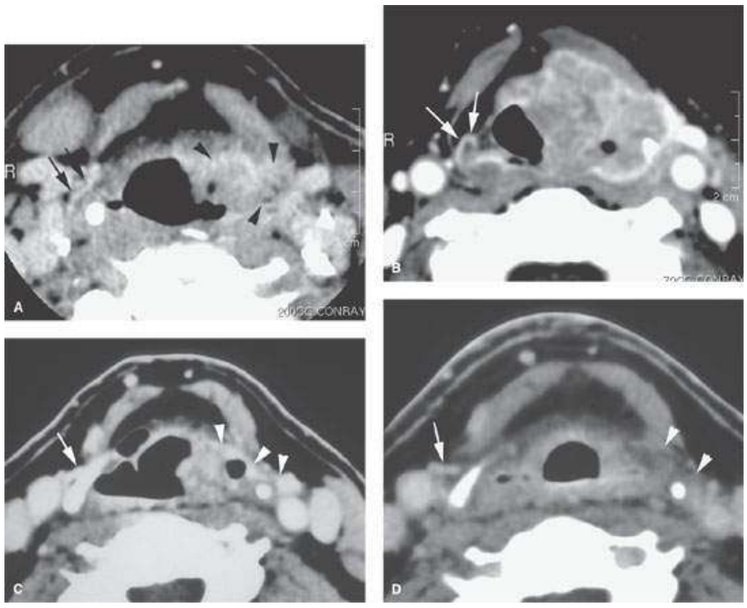


FIGURE 206.17. Contrast-enhanced computed tomography study of three patients with marginal supraglottic lesions showing a tendency for the lesions to spread out of the larynx through an area of inherent weakness along the region of penetration of the superior laryngeal neurovascular bundle. A: Patient 1. A highly infiltrating–appearing lesion (arrowheads) involves the infrahyoid strap muscles and grows to surround veins in the deep neck compared to the normal superior laryngeal vascular bundle on the opposite side (arrow). B: Patient 2 with a tumor that has more pushing type of margins but showing the same tendency to grow out of the larynx along the superior laryngeal neurovascular bundle. Note the normal superior laryngeal vessels as they penetrate the thyrohyoid membrane on the right (arrowheads). C, D: Patient 3 showing spread of tumor along the superior laryngeal neurovascular bundle toward the carotid artery in the left neck (arrowheads) compared to the normal vessels on the right side (arrow). This was a relatively low volume lesion treated with radiotherapy (RT). In (D), following RT, there is restoration of the normal anatomy around the superior laryngeal vessels (arrowheads) except for some vague soft tissue swelling. (Note: The normal vessel on the right (arrow). These are minor post-RT changes seen within the larynx. The patient was controlled with RT alone.)

Subglottic spread may occur along the mucosa and be easily seen endoscopically. However, spread may also be directed beneath the mucosa on either side of the conus elasticus (Figs. 206.3, 206.6A, 206.7, and 206.21); therefore, subglottic spread may not be visible at the time of staging endoscopy. Ten to 15 mm of subglottic spread anteriorly or 4 to 5 mm of subglottic spread posteriorly brings the tumor edge to the upper margin of the cricoid. Preservation of the cricoid is critical to most surgical plans that restore normal or near-normal glottic function, although partial resection of the cricoid with preservation of function is possible.[10]

Deep spread of more advanced TVC cancer will extend to the ventricle/FVC, vocal process of the arytenoid, and subglottic region (Figs. 206.6A, 206.7, 206.9, 206.14, and 206.19–206.22). Infiltrative lesions invade the vocal ligament and muscle and eventually reach the paraglottic space and then the perichondrium of the thyroid cartilage. Once a glottic cancer reaches the perichondrium of the thyroid lamina, it grows vertically along that lamina within the paraglottic space rather than preferentially invading the cartilage. The conus elasticus directs but does not restrain subglottic growth. The conus elasticus may influence tumor growth toward the cricothyroid membrane. These glottic cancers may penetrate the thyroid cartilage, cricothyroid membrane, and/or cricoid cartilage and spread to the neck where they can invade the thyroid gland and other soft tissues. TVC cancers invading the anterior commissure particularly tend to grow through the cricothyroid membrane after they extend to the subglottis. Anterior subglottic spread through the cricothyroid membrane is frequently associated with invasion of the adjacent margins of the thyroid or cricoid cartilages (Fig. 206.20). Such growth is also associated with a higher rate of involvement of the prelaryngeal group of level 6 nodes. Also, at times, this growth pattern makes it necessary to perform a lower than usual tracheostomy to avoid placing the tracheostomy through tumor; imaging before tracheostomy helps to anticipate this uncommon situation that can have detrimental effects on outcome if not recognized (Figs. 206.2 and 206.23).

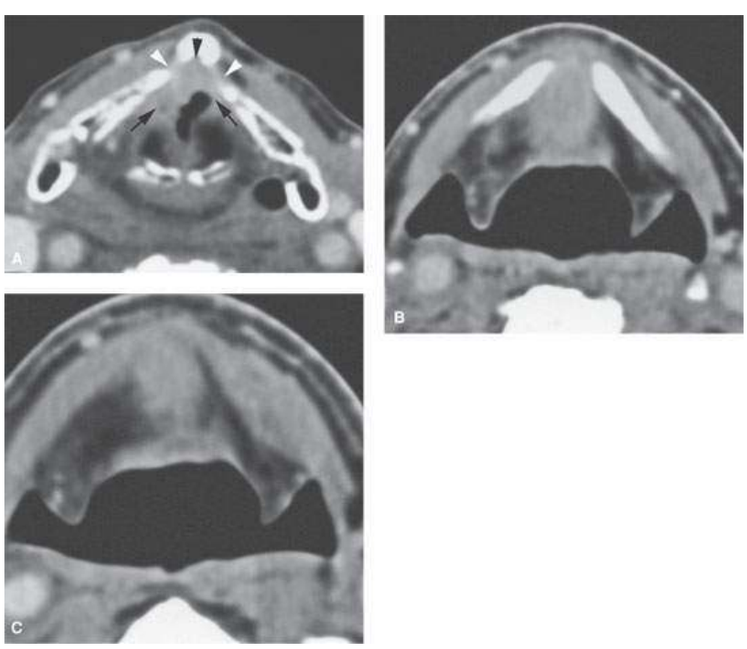


FIGURE 206.18. Contrast-enhanced computed tomography (CECT) study of a patient with laryngeal carcinoma arising at the anterior commissure. Most of the spread of this tumor was submucosal. A: CECT done just above the level of the true cords shows infiltrating tumor bilaterally (black arrows) in the anterior aspect of the paraglottic space extending to just above the anterior commissure (black arrowhead). There are areas of symmetric normal variation in

mineralization of the thyroid cartilage versus evidence of earlier cartilage invasion (white arrowheads). B: Bulky tumor is seen more superiorly in the pre-epiglottic space extending into the thyroid notch. C: Continued spread of tumor superiorly in the pre-epiglottic space. (NOTE: While anterior commissure carcinomas are relatively rare, they frequently have substantial amounts of tumor growing submucosally that will alter the therapeutic plan. This is such an example.)

Subglottis

Primary subglottic cancers are rare. Most have invaded the TVCs by the time of diagnosis. This makes it difficult to determine whether the tumor started on the patients undersurface of the vocal cord or in the subglottis. Subglottic primaries are usually bilateral or circumferential in most by the time they come to imaging (Figs. 206.2, 206.6C, 206.7, and 206.19) Subglottic cancers frequently invade the cricoid cartilage since they grow along the conus elasticus to its cartilage attachments (Fig. 206.24). They penetrate the cricothyroid membrane early with tumor extending into the anterior soft tissues of the neck and/or through the cricothyroid membrane to invade the thyroid gland. Growth to the undersurface of the TVCs with TVC fixation is common. Tracheal extension occurs frequently.

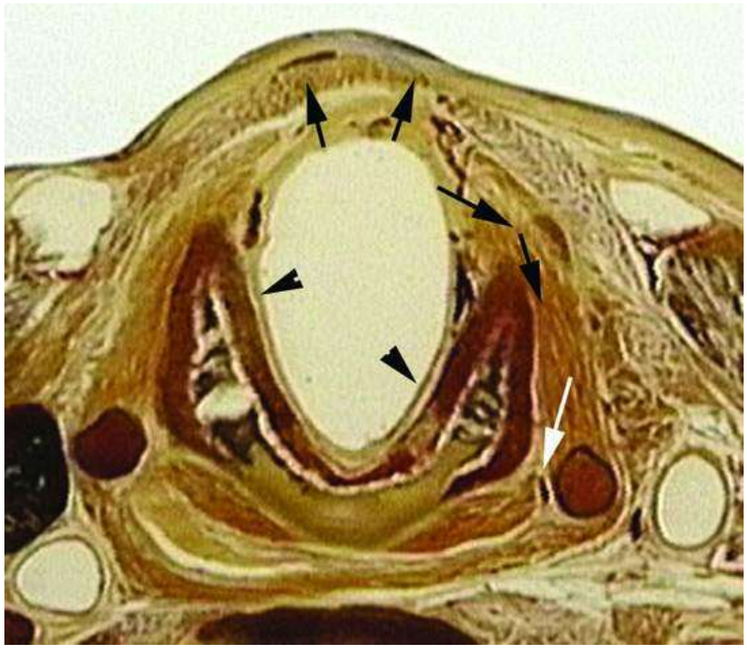


FIGURE 206.19. Whole organ section demonstrating potential pathways of spread of glottic cancer through the cricothyroid membrane into the soft tissues of the neck anteriorly as well as laterally (black arrows), where they may extend inferiorly into the thyroid gland and even the cervical esophagus. This also demonstrates the very minimal soft tissue changes usually present along the inner surface of the cricoid cartilage (black arrowheads) as well as the expected point of penetration of the recurrent laryngeal nerve and associated inferior thyroid artery branches to the larynx (white arrow). This is located usually at the lower aspect of the joint between the inferior cornu of the thyroid cartilage and the cricoid cartilage.

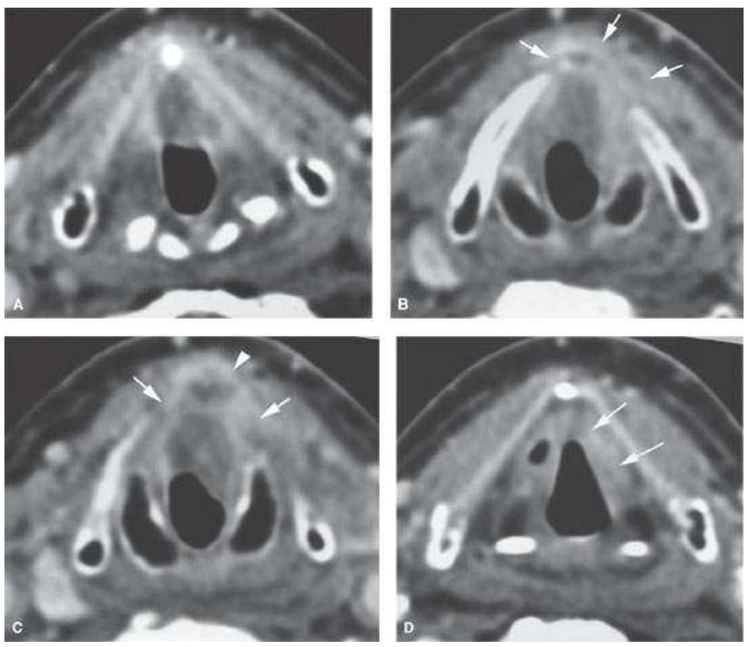


FIGURE 206.20. Contrast-enhanced computed tomography study of a cancer at the anterior commissure. The tumor was originally treated with radiotherapy for cure. Its extent may have been originally underestimated. The patient presented to us with recurrent hoarseness and pain for further evaluation and treatment. On physical examination, there was no definite mucosal disease. A: A bulky mass is present at the anterior commissure. B: Just below the anterior commissure, the mass appears to erode through the undersurface of the thyroid cartilage into prelaryngeal soft tissues (arrows). C: There is continued subglottic spread and spread into the prelaryngeal soft tissues (arrows). D: Cephalad spread to the paraglottic space at the level of the false cord was also present (arrows).

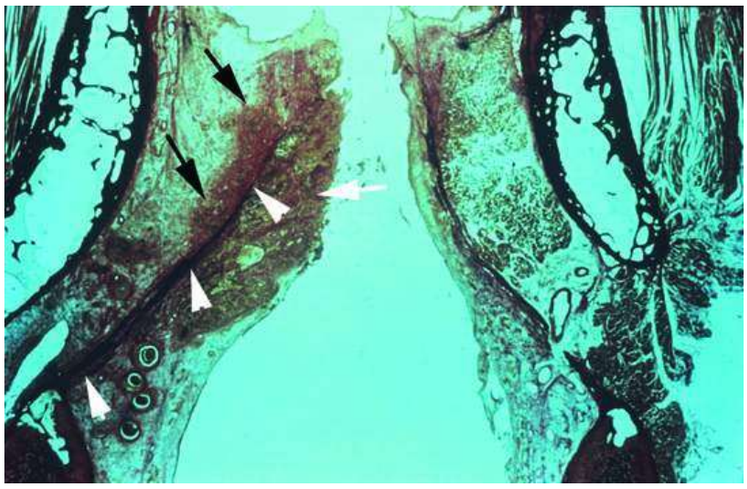


FIGURE 206.21. Whole organ coronal section showing how a very infiltrative tumor may spread relative to the conus elasticus (white arrowheads). This tumor spreads both deep (black arrows) to the conus and along the mucosal surfaces (white arrow) superficial to the conus elasticus.

Lymphatic Spread

Supraglottis

The distribution and frequency of cervical lymph node metastases from SCCA of the supraglottic larynx are presented in Figure 206.25. The spread pattern is mainly to levels 2 and 3 of the internal jugular nodes. Level 1 is rarely involved. There is minimal risk of level 5 lymph node involvement.

The general incidence of clinically positive nodes is 55% at the time of diagnosis. Clinically positive cervical lymph node metastases occur bilaterally in about 15% of patients; that percentage increases to 25% based on elective neck dissection data. Observation of a clinically negative neck (by physical examination) will be followed by the appearance of positive nodes in a significant number of patients. Ten percent of the positive nodes will be in level 6. Extralaryngeal spread, including that to the pyriform sinus and vallecula/base of the tongue, increases the risk of nodal metastases. The risk of contralateral adenopathy approaches 40% if the ipsilateral neck is positive clinically or surgically.

Vocal Cord and Subglottic Primaries

Clinically positive lymph nodes at the time of presentation for a truly T1 glottic cancer is rare and is only seen in 2% to 7% for T2 cancers. This is related to the usually indolent biology of the cancers and the sparse capillary lymphatics of the TVC.

T3 and T4 carcinomas have a 15% to 20% risk of cervical lymph node metastases (Fig. 206.26). This risk has been proven by neck dissection in patients with clinically negative necks. Ipsilateral level 2 and 3 nodes are at highest risk with about 18% to 20% risk of level 6 involvement. Levels 1 and 5 are almost never involved. Spread to the FVC and more superiorly raises the risk of level 2 metastases. Anterior subglottic spread raises risk for levels 4 and 6. The neck is typically controlled even if involved in patients with glottic cancer. The current edition of the American Joint Committee on Cancer (AJCC) guidelines changes the staging of mobile TVC cancer with paraglottic space invasion, placing those cancers in the T3 category. This will result in stage migration.

Primary subglottic cancers have a high risk of level 6 and, to a lesser extent, level 4 nodal metastatic disease.

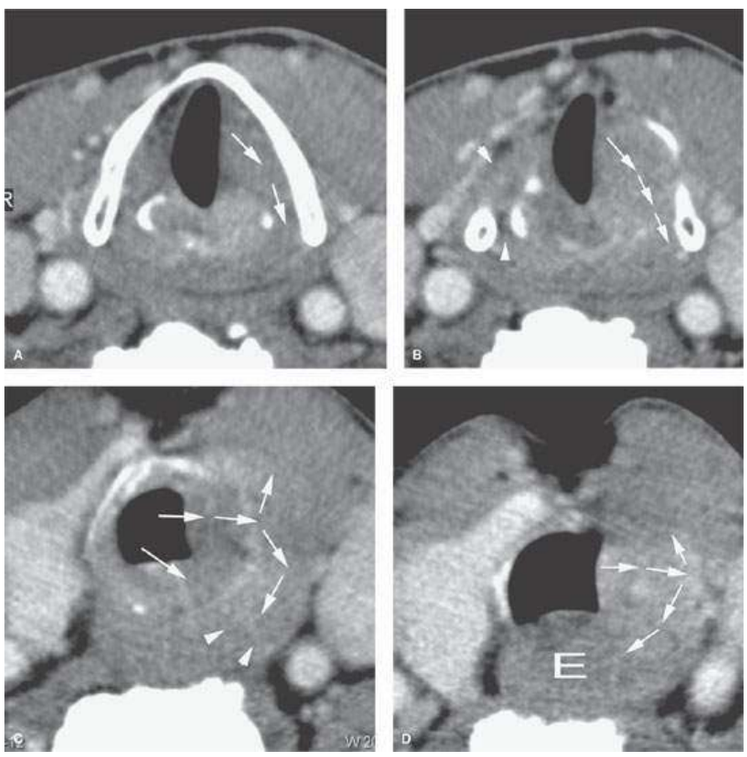


FIGURE 206.22. A clinically T3 carcinoma of the true vocal cord. This study shows the cancer to be much more extensive. A: At the undersurface of the true cord, cancer spreads from the true cord to the interval between the cricoid and thyroid cartilages (arrows). B: In the mid subglottis, continued spread between the cricoid and thyroid cartilage is present (arrows) compared to the normal anatomy on the opposite side (arrowheads). C: In the lower subglottis, the extensive endoluminal mass grows into the soft tissues of the neck in all directions, including likely invasion of the postcricoid portion of the hypopharynx (arrowheads). D: Section at the level of the trachea showing tumor spreading predominantly in the extralaryngeal soft tissues to invade the thyroid gland (arrows) and cervical esophagus (E). E: Coronal reformations showing the extent of endoluminal tumor (white arrows). Spread of tumor outside of the larynx is demonstrated by the black arrows. Tumor invades the upper pole of the thyroid gland (black arrowheads). Note the normal first three tracheal rings on the right side (white arrows) below the cricoid cartilage (C). This indicates that tumor had spread as low as the third tracheal ring on the side of involvement. (NOTE: Such imaging findings dramatically alter the approach to patient care in what was originally believed to be a possibly limited true cord tumor.) F: Whole organ section demonstrating potential routes of both mucosal (black arrowheads) and submucosal spread of true vocal cord cancer (white arrows).

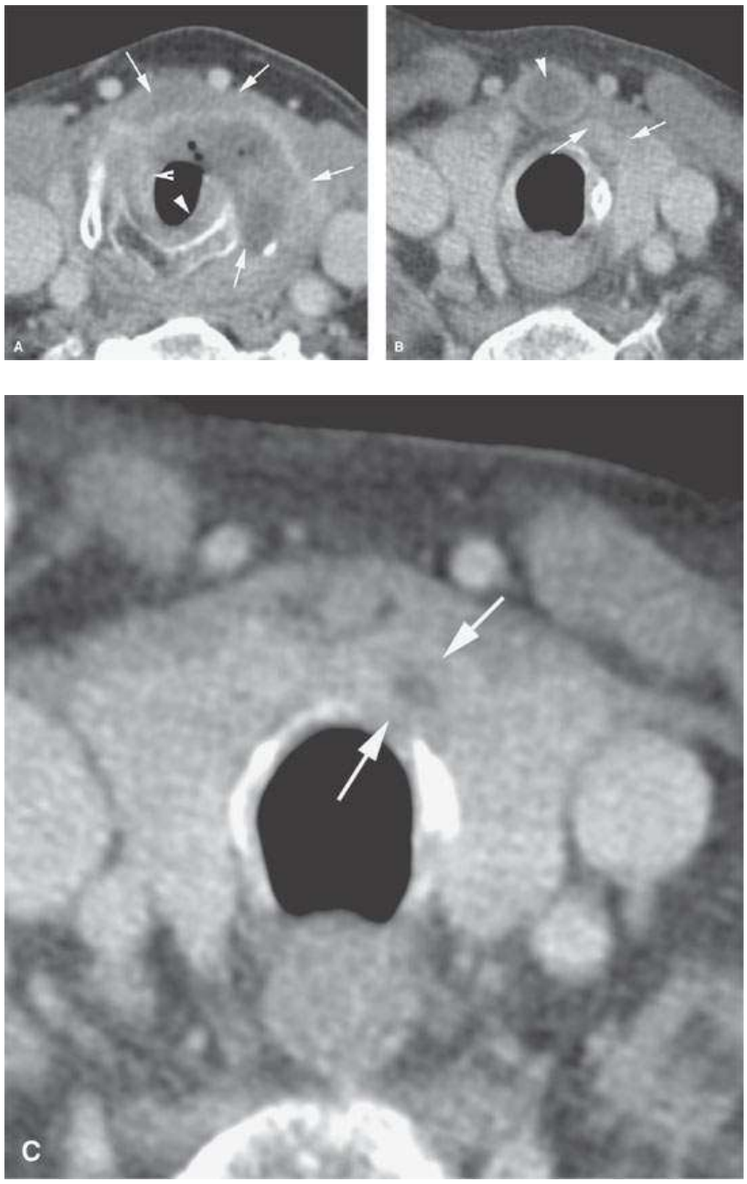


FIGURE 206.23. Contrast-enhanced computed tomography study of a patient presenting with acute respiratory distress due to advanced laryngeal carcinoma. The tumor arises on the true vocal cords. A: The mid subglottis is filled with tumor (arrowheads), which spreads extensively outside the larynx. B: Tumor had spread to a prelaryngeal level six lymph node (arrowhead) as well as directly to the soft tissues of the neck around the thyroid isthmus (arrows). This image is at the level of the first tracheal ring. C: An image at the level of the second tracheal ring remains suspicious for tumor spread outside the larynx and involvement of the tracheal ring (arrows). This image was at the level of the second tracheal ring. (NOTE: If possible, diagnostic imaging should be obtained before tracheostomy in patients with advanced laryngeal carcinoma. In this patient, imaging helped decision making with regard to placing the tracheostomy tube lower than usual to avoid its passing through gross tumor.)

Staging

The AJCC and International Union Against Cancer (UICC) staging systems for laryngeal cancer are identical. Note that cancers of the supraglottis include those arising on the false cords, aryepiglottic folds, suprahyoid epiglottis, and infrahyoid epiglottis. Once lesions enlarge, it may be difficult to identify the specific site

of origin. Imaging patterns of spread are sometimes more revealing than the clinical examination in this situation.

The prime determinants of more advanced disease are spread to more than one of the three laryngeal regions; TVC fixation; and spread beyond the larynx, especially through the framework and into the soft tissues of the neck.

Cartilage invasion is an important factor as well. Caveats with regard to assessing early macroinvasion were discussed in the contraversies of this chapter under the heading Cartilage Invasion.

The lower boundary of the glottic level according to the AJCC is 1 cm below the apex of the laryngeal ventricle. Some groups define the glottic–subglottic junction as 5 mm below the free margin of the mid TVC.

Spread inferiorly beyond the cricotracheal junction is considered tracheal extension.

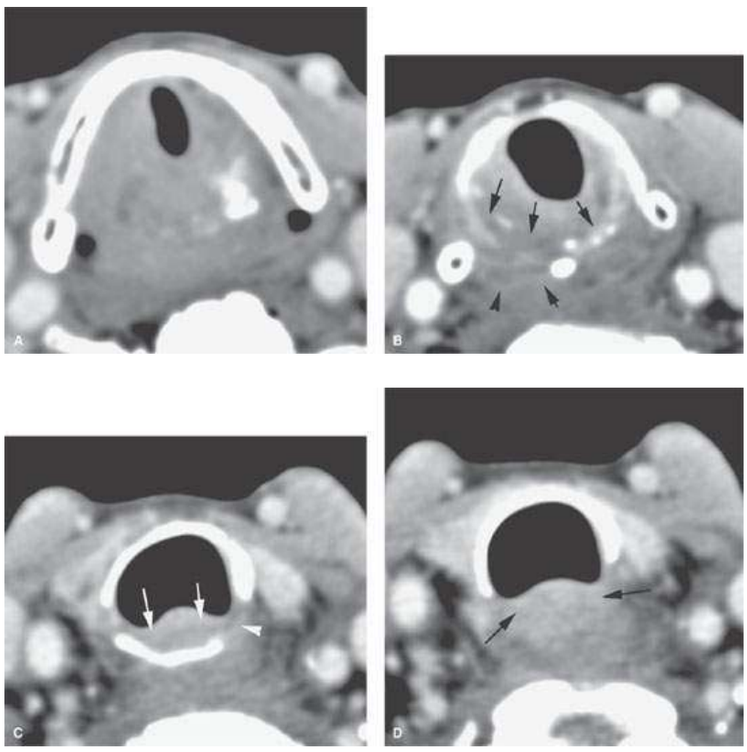
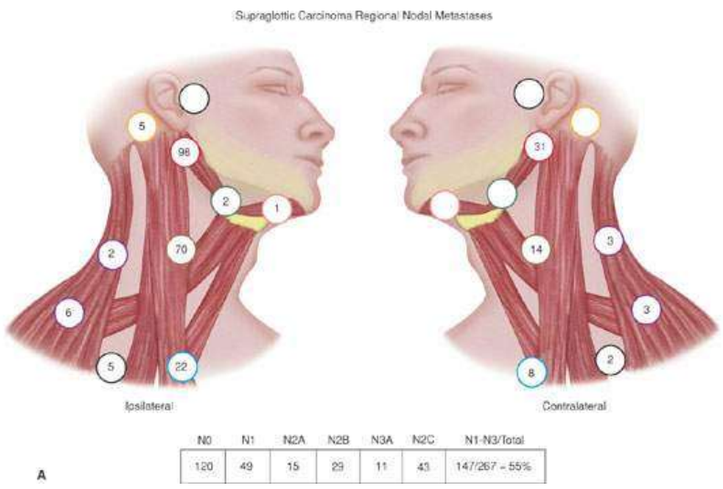


FIGURE 206.24. Contrast-enhanced computed tomography study of a patient with primary subglottic carcinoma. A: Extensive tumor eroding the cricoid and arytenoid cartilage at the level of the true cords. B: Subglottic tumor extensively invading the cricoid lamina (arrows) to involve the muscular wall of the postcricoid hypopharynx (arrowheads). C: At the lower margin of the cricoid lamina, there is still gross tumor (arrows) extending into the soft tissues of the neck (arrowhead). D: At the level of the first tracheal ring there is still evidence of tumor involving the common wall between the trachea and esophagus and fairly extensive edema in the surrounding fat (arrows). (Note: MRI would better determine the lower extent of the cancer if necessary for clinical decision making. This is discussed in more detail in Chapter 219.)



N0	N1	N2A	N2B	N3A	N2C	N1-N3/Total
120	49	15	29	11	43	147/267 = 55%

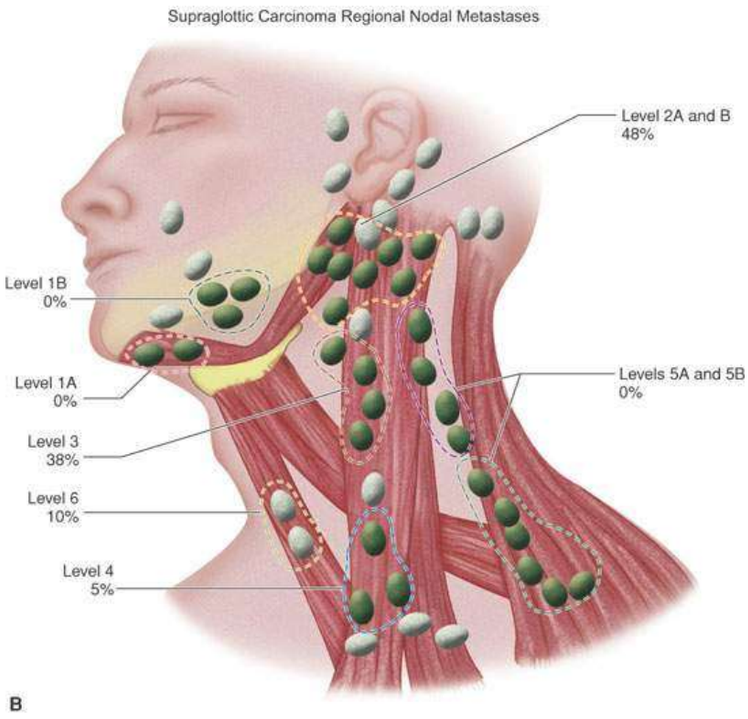


FIGURE 206.25. Diagrams showing the risk of metastases in patients with supraglottic carcinoma. (Part A is modified from Lindberg R. Distribution of cervical lymph node metastases from squamous cell carcinoma of the upper respiratory and digestive tracts. Cancer. 1972;29:1446–1449. Part B is modified from Byers RM, Wolf PF, Ballantine AJ. Rationale for elective modified neck dissection. Head Neck Surg. 1988;10:160–167.)

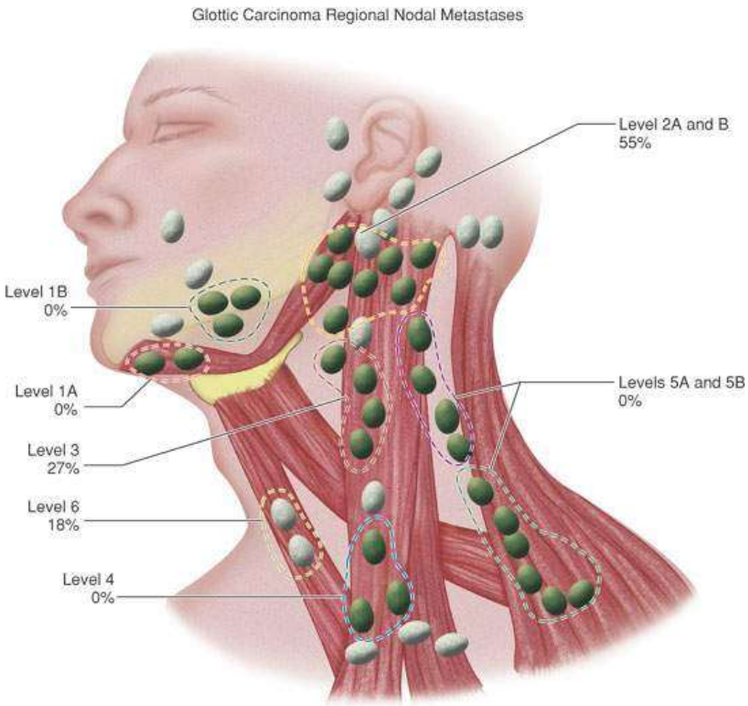


FIGURE 206.26. Diagram showing the rate of regional nodal metastases in glottic carcinoma. (Modified from Byers RM, Wolf PF, Ballantine AJ. Rationale for elective modified neck dissection. Head Neck Surg. 1988;10: 160–167.)

Manifestations and Findings

Plain Film and Fluoroscopy

Plain film and fluoroscopy are not typically used to evaluate the laryngeal region. Laryngeal and hypopharyngeal cancer may be diagnosed inadvertently on swallowing examinations performed for dysphagia or odynophagia or on those who might be aspirating.

A plain film of the chest is routinely used to search for lung metastasis or synchronous primary lung neoplasm.

Computed Tomography and Magnetic Resonance Imaging

CECT and CEMR will show infiltrating lesions involving the mucosal structures and deep planes in and around the larynx described in the patterns of spread section. The cancers range from superficially spreading and/or entirely exophytic to mainly endophytic and sometimes entirely submucosal. Cartilage invasion is manifest and evaluated in a manner also described in those sections and in the sections on controversies. The areas of infiltrating tumor will usually enhance more than muscle, perhaps quite a bit more, but primary lesion morphology can vary considerably as discussed in Chapters 21 and 23. Generally, deeply infiltrating tumor will invade muscles, replace fat, and may spread along neurovascular bundles (Fig. 206.17) or natural areas of weakness in the laryngeal skeleton. The details of how these mucosal lesions spread and tend to appear on CECT and CEMR are discussed in conjunction with general tumor growth patterns and those of epithelial tumors of mucosal origin in Chapters 21 and 23.

The findings in regional lymph node disease are discussed in conjunction with cervical metastatic disease in Chapter 157.

Ultrasound

Ultrasound has no role in the staging of a laryngeal cancer primary site. The ultrasound findings in regional lymph node disease are discussed in conjunction

with cervical metastatic disease in Chapter 157.

Nuclear Medicine

In most laryngeal carcinomas, the tumor and related nodal metastases will be hypermetabolic. This must be differentiated from areas of physiologic uptake and coincidental inflammatory and sometimes unrelated neoplastic hypermetabolic activity.

Catheter Angiography

Catheter angiography is rarely used to evaluate a hypervascular laryngeal tumor, such as a suspected paraganglioma (Fig. 33.7 and Chapter 205). It may also be used to deliver intra-arterial chemotherapy in combination with RT for the treatment of advanced laryngeal cancer.

Endoscopy

Indirect laryngoscopy or fiber-optic endoscopy is initially performed in the office. Direct laryngoscopy and biopsy are performed with the patient under general anesthesia for a definitive diagnosis. The endoscopist will biopsy the obvious lesion and any other suspicious areas. Aside from the primary and suspicious areas, the mucosa of the ventricles, subglottis, apex of the pyriform sinus, and postcricoid area are examined carefully since these areas are not consistently seen by any other method. In a similar manner, the diagnostic imager should evaluate these areas for contiguous spread or a second primary.

Differential Diagnosis

From Clinical Data

The differential diagnosis of early laryngeal cancer includes papillomas, polyps, vocal nodules, fibromas, and granulomas. Papillomas occur in children and young adults. Laryngeal cancer is a disease essentially of older smoking adults, but laryngeal papillomatosis predisposes children to this disease. Vocal polyps and vocal nodules occur in the mid TVC due to voice abuse.

Traumatic granulomas are most commonly the result of intubation and are located posteriorly at the glottic level.

Tuberculosis, syphilis, and other infections discussed in Chapter 204, as well as other nonneoplastic diseases such as sarcoidosis (Chapter 18), amyloidosis, and other immune-mediated diseases (Chapter 20), can rarely mimic cancer. This is almost never anticipated, with the nature of the disease being revealed at biopsy.

Other benign masses can mimic cancer, and these are discussed in more detail in conjunction with those benign tumors of laryngeal origin discussed in Chapter 205.

From Supportive Diagnostic Techniques

The differential diagnosis is usually not altered by laboratory findings. If the imaging pattern is diffusely infiltrating and suggesting an alternative tissue diagnosis such as lymphoma (Fig. 27.12 and Chapter 27), such testing may suggest Wegener granulomatosis (Fig. 17.11 and Chapter 17), sarcoidosis (Fig. 18.10 and Chapter 18), or amyloidosis (Figs. 20.16–20.18 and Chapter 20).

Imaging may provide clues or at times a specific diagnosis as follows:

- Laryngeal chondrosarcoma may show an obvious origin from cartilages with a possible characteristic chondroid matrix (Figs. 39.5–39.7).
- A well-circumscribed mass that appears as if it might be submucosal that enhances considerably is suggestive of a sarcoma (Fig. 35.10). A similar mass with cystic or necrotic zones suggests a salivary or neurogenic tumor (Fig. 27.14).

Definitive diagnosis is by endoscopic biopsy or occasionally at the time of definitive surgical resection. Percutaneous imaging-guided biopsy can be an effective approach when endoscopic biopsy is unsuccessful and the mass is not palpable or, for some other reason, cannot be safely approached without such guidance.

Medical Decision Making and Treatment Options

Medical

Chemotherapy is commonly used in conjunction with surgery and/or RT in advanced or recurrent disease. This is discussed in more detail in the following sections on surgical and RT management.

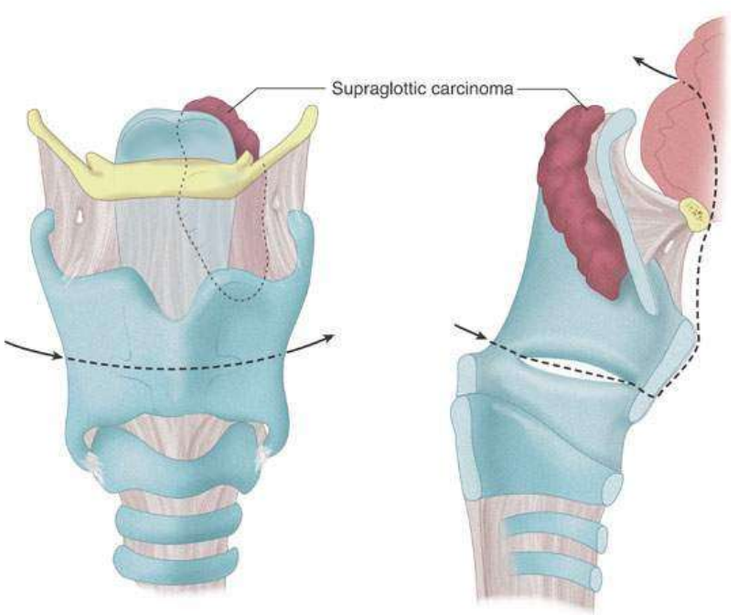


FIGURE 206.27. Diagram of basic margins of resection required for supraglottic laryngectomy.

Surgical

Supraglottic Cancer

Supraglottic cancers can be triaged to an early or favorable group suitable for control with voice preservation by RT and an unfavorable group that may require

total laryngectomy. Cervical node metastases are common, and this risk often influences the treatment strategy.

Early supraglottic cancer may be treated by either RT or supraglottic laryngectomy (Fig. 206.27). Total laryngectomy is reserved for advanced primaries or salvage of initial treatment failures. Chemoradiation protocols can be used in advanced primaries if the patient cannot accept the loss of the larynx as an initial strategy.

Supraglottic laryngectomy is a voice-sparing operation that can be used successfully for selected lesions. There are no randomized data comparing supraglottic laryngectomy and RT, but comparing nonrandomized data, supraglottic laryngectomy probably produces a higher local control rate. However, this procedure has a higher risk of complications compared with RT, mainly related to swallowing difficulties and aspiration. Suitability for supraglottic laryngectomy depends on the extent and anatomic location of the tumor discussed subsequently; however, it also depends on the medical condition of the patient. Patients with pulmonary or cardiac disease are not good candidates for this procedure because essentially all patients aspirate to some degree after the operation. It is estimated that the proportion of patients suitable for conservative surgery in an unselected population is about 15% to 20%.

Supraglottic laryngectomy can only be performed if the TVC, anterior commissure, and laryngeal ventricles are not involved. Tumor should be 3 mm from the anterior commissure. There must not be involvement of both arytenoids or cricoid or thyroid. The supraglottic laryngectomy may include the base of the tongue in lateralized lesions where one lingual artery can be preserved.

The structures removed in supraglottic laryngectomy include the epiglottis, FVCs, the aryepiglottic folds, and the pre-epiglottic space. The supraglottic region of the thyroid cartilage is also resected. The hyoid bone may be partially resected, but supraglottic laryngectomy with preservation of the hyoid bone may also be performed. One arytenoid may be sacrificed. These factors must be taken into account when evaluating postoperative images in such patients (Fig. 206.27).

Reduced mobility and fixation of the vocal cord are contraindications to supraglottic laryngectomy. An imaging correlate for these findings may be submucosal spread to the TVC level via the paraglottic space. Local control rates diminish in this group compared to those for patients with normal vocal cord mobility.

Highly infiltrative behavior and occult spread beyond the limits of supraglottic laryngectomy may only be visible on CT or MRI. Invasion of the pre-epiglottic space is not a contraindication to supraglottic laryngectomy; the chances to obtain cure by RT decrease with increasing infiltration of the pre-epiglottic space. This may be related to this aspect of the tumor being relatively underperfused and therefore less oxygenated.

The preferred treatment for most T1, T2, and favorable T3 supraglottic lesions is RT. Most of these patients require elective irradiation of both sides of the neck since supraglottic cancers are prone to metastasize bilaterally. In supraglottic cancer, the status of the neck frequently determines the selection of treatment of the primary lesion. Patients with a clinically negative neck but high risk for subclinical bilateral neck disease may be treated by RT because of the ease of bilateral elective neck irradiation. The alternative treatment would be supraglottic laryngectomy and bilateral modified neck dissections.

Patients with a favorable primary lesion but advanced neck disease (N2B or N3) often require RT and surgery to achieve an acceptable control rate of the neck disease. In such cases, the primary lesion may be treated for cure by irradiation, and neck dissection is added if there is concern of incompletely treated residual nodal disease. If there is early, resectable neck disease and surgery is chosen for the primary site, then postoperative irradiation may also be added if there is extracapsular spread, more than one positive node, perineural invasion, or close margins.

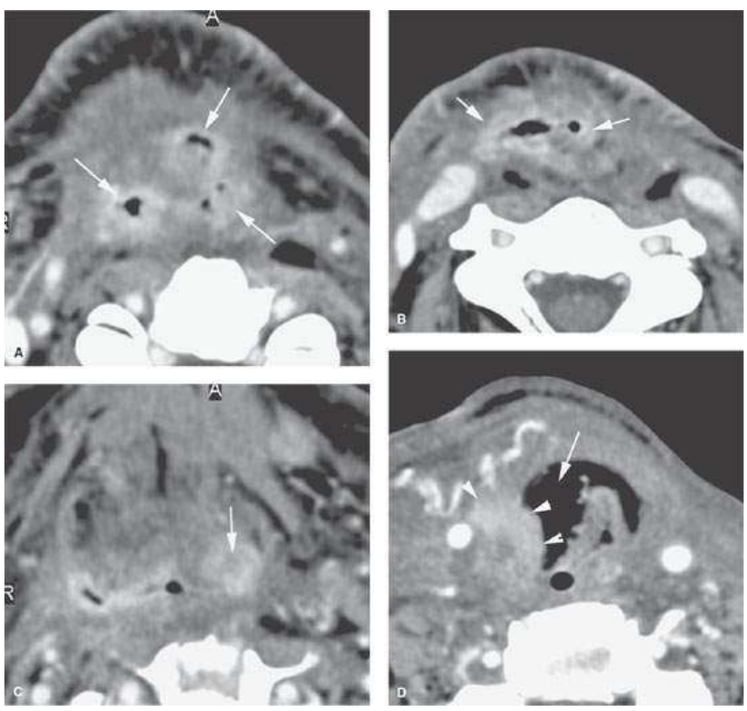


FIGURE 206.28. Two patients treated with total laryngectomy for squamous cell carcinoma who failed radiation therapy. Both patients had dysphagia. A–C: Patient 1 reconstructed with routine creation of a neopharynx. There is multifocal recurrent tumor throughout the neopharynx that extends into the lower left glossotonsillar sulcus (arrows). D: Patient 2 with flap reconstruction used to create the neopharynx. The fat of the flap that reconstructs the anterior pharyngeal wall is easily visible (arrow). At the interface between this flap and the soft tissues of the neck, there is an enhancing recurrent carcinoma (arrowheads).

Advanced supraglottic cancer is most often treated with total laryngectomy. If resectable neck disease is present, surgery comes first and RT as indicated. If the neck disease is unresectable, preoperative irradiation may be used. Unfavorable but less advanced lesions may be treated with chemoradiation. Imaging may be critical for categorizing very advanced disease as being based primarily on very high volume and/or clinically occult spread to the tongue base or laryngeal framework, or transglottic or extralaryngeal spread to the soft tissues of the neck.

Supraglottic laryngectomy or RT failure can frequently be salvaged by further treatment (Fig. 206.12). Selected high-risk patients should undergo anatomic (imaging) or FDG-PET surveillance to assure the earliest recognition of failure. Stomal recurrences are unusual. Failure after laryngectomy will occur at the margins of the neopharynx of flap used for reconstruction, usually the mid to upper portions of the construct (Fig. 206.28).

Glottic and Subglottic Cancer

The goal of treatment is almost always cure with the best functional result while minimizing risk of a serious complication. Treatment for palliation only at this primary site is very unusual. Early glottic cancer (T1 and T2) may be treated initially by RT or partial laryngectomy or transoral laser resection depending on the location and extent of the tumor. Late glottic cancer can be treated with RT, reserving laryngectomy for failure, or by total laryngectomy possibly followed by RT.

T3 glottic lesions may be subdivided into favorable lesions suitable for a voice preservation strategy and unfavorable lesions. Favorable T3 glottic cancer usually involves one side of the larynx and does not threaten the airway. T3 glottic cancer can be further risk stratified by CT. Tumors, 3.5 cc volume and with one or no sclerotic cartilages are 90% likely to be cured with voice preservation by RT. Tumors with a volume of 3.5 cc and one or no sclerotic cartilages have a control rate of 40% to 60%, and those with tumors .3.5 cc and two or more sclerotic cartilages are, 10% likely to be cured with RT alone4 (Fig. 206.29).

Higher-risk patients may be treated with concomitant chemoradiation protocols if nonsurgical treatment fails, reserving laryngectomy for salvage. Some surgeons may elect to treat selected T3 cancers with extended vertical hemilaryngectomy.

Most extensive T3 and nearly all T4 lesions require treatment with total laryngectomy, with or without postoperative irradiation (Fig. 206.15). The addition of neck dissection is evaluated on a case-by-case basis. A clinically negative neck will not require neck dissection if postlaryngectomy RT to both necks is planned. When postoperative RT is not planned, an elective neck dissection is done. Frequent sites of local failure after total laryngectomy are at the tracheal stoma and tongue base (Fig. 206.30).

For vertical hemilaryngectomy, the maximum subglottic extension allowable is 8 to 9 mm anteriorly and 5 mm posteriorly so that an adequate margin with cricoid preservation is possible. Tumor extension to the epiglottis, FVC, or both arytenoids is a contraindication to hemilaryngectomy (Fig. 206.31). Imaging is critical for identifying occult spread to areas that might exclude partial laryngectomy as a treatment option. More extensive lesions may sometimes be treated by supracricoid laryngectomy.

Total laryngectomy removes the entire larynx, and the pharynx must be reconstituted by creating a “neopharynx.” The trachea is sutured to the skin, establishing a permanent tracheal stoma (Fig. 206.32).

Subglottic cancer is most commonly advanced at presentation and treated with total laryngectomy, and postoperative irradiation is added as indicated. For early disease, the cure rate for irradiation with laryngectomy reserved for local failure is equivalent to laryngectomy.

Radiotherapy

Supraglottic Cancer

Supraglottic cancers can also be triaged to an early or favorable group suitable for control with voice preservation by RT alone that may require total laryngectomy. Cervical node metastases are common, and this risk often influences the treatment strategy.

Low-volume supraglottic cancer is preferably treated by RT if the patient is not a candidate for supraglottic laryngectomy either for technical or functional capacity reasons as discussed in the preceding section (Figs. 206.11 and 206.12).

Irradiation and supraglottic laryngectomy are both highly successful in treating early primary cancers, so a combined RT/surgery is normally not necessary for initial management of the primary lesion. Combined treatment may be necessary to control the neck disease.

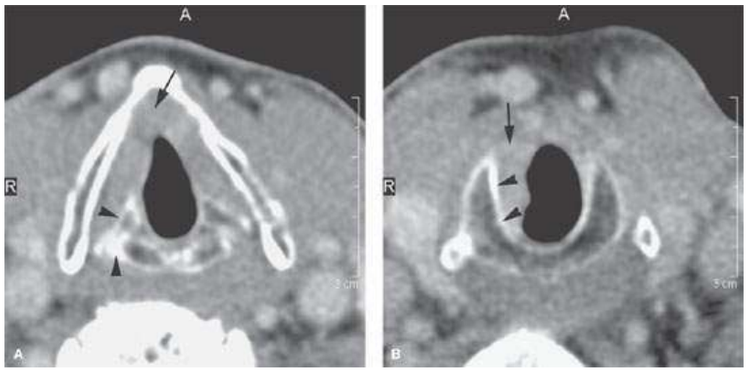
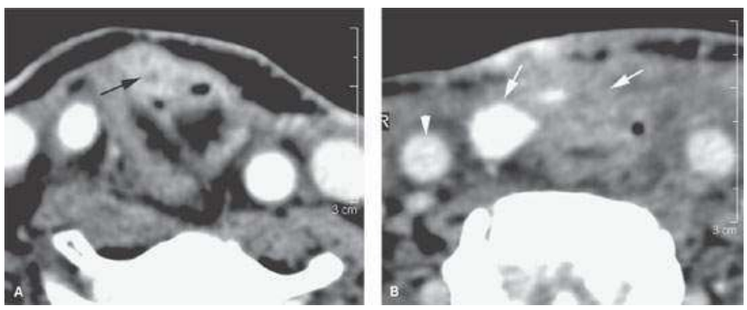


FIGURE 206.29. A patient with T3 glottic carcinoma. A contrast-enhanced computed tomography study was done. A: Right true vocal cord cancer with thickening of the anterior commissure (arrow) and sclerosis of the arytenoid cartilage and superior margin of the cricoid cartilage (arrowheads). B: The patient had approximately 12 mm of subglottic spread. The section through the lower subglottis shows the endoluminal tumor (arrow) and sclerosis of the adjacent cricoid cartilage. (NOTE: Tumor volume was slightly .3.5 cc; that combined with two sclerotic cartilages made this tumor high risk to fail radiotherapy [RT]. The patient elected for RT. Chemotherapy was also given. Treatment failed, and the patient was successfully salvaged with total laryngectomy, with the early failure picked up by surveillance anatomic imaging [not shown]).



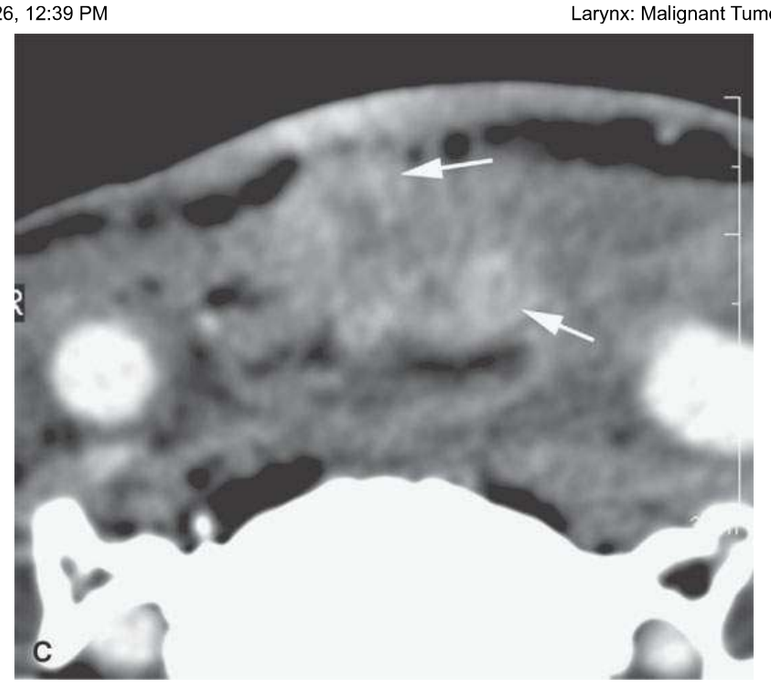


FIGURE 206.30. Contrast-enhanced computed tomography of two patients with neopharyngeal recurrence. A: Patient 1 with a relatively normal-appearing neopharynx except for a nodule of recurrent tumor (black arrow). The patient presented with dysphagia. B, C: Patient 2. In (B), a relatively extensive infiltrating mass involves the residual thyroid gland and anterior wall of the neopharynx (arrows). The carotid artery (arrowhead) is free of disease. In (C), multifocal areas of involvement are present at another level (arrows).

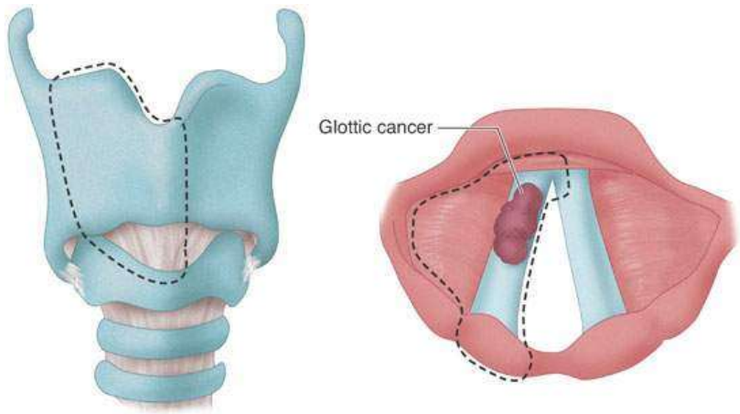


FIGURE 206.31. Diagram showing the extent of a vertical hemilaryngectomy procedure.

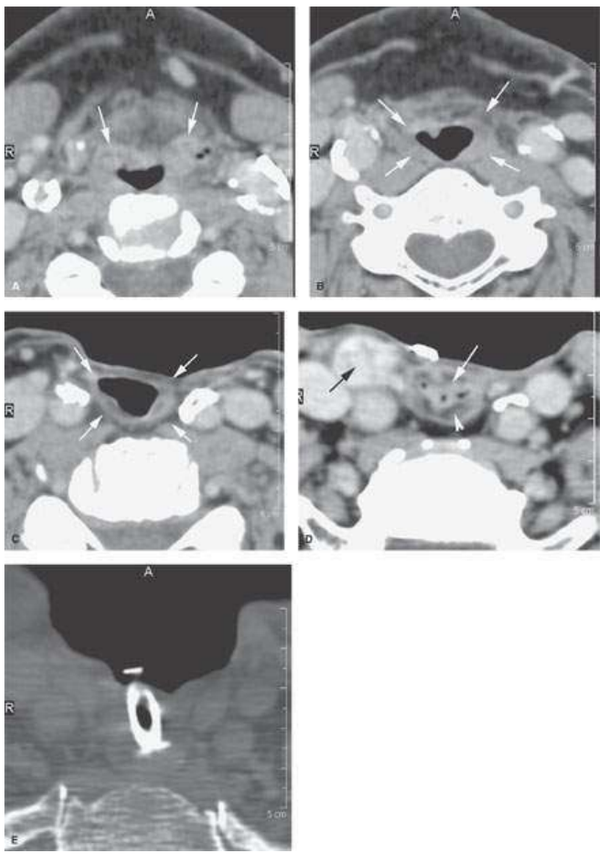


FIGURE 206.32. Contrast-enhanced computed tomography of a patient who had laryngectomy for laryngeal carcinoma and reconstruction of the pharynx by primarily closing the residual pharyngeal wall. This is the most common form of reconstruction of a neopharynx following laryngectomy. A–D: The margins of a normal-appearing neopharynx and relatively normal surrounding soft tissues are demonstrated by the arrows. In (D), the residual thyroid gland preserved for both thyroid and parathyroid function on the right side happens to contain a benign nodule (arrow). The neopharynx at that level has an appearance consistent

with “gut,” with a musculature wall (arrowhead) and enhancing mucosal surface (white arrow). E: The stoma site is demonstrated with a tracheoesophageal puncture and a valve placed for voice rehabilitation.

Treatment of larger volume and infiltrative lesions may be preferentially selected for supraglottic laryngectomy combined with postoperative irradiation. Imaging is critical in this decision making. Highly infiltrative behavior and occult spread beyond the limits of supraglottic laryngectomy may only be visible on CT or MRI (Fig. 201.13).

Invasion of the pre-epiglottic space is not a contraindication to supraglottic laryngectomy or RT.

More specific risk stratification for likelihood of RT control with voice preservation is possible based on imaging. Tumor volume is almost linearly related to RT control in supraglottic primaries.[11,12] Measurement of tumor volume has proved to be a relatively simple method easily mastered by radiologists and radiation oncologists who understand laryngeal cancer. Patients with T1 through T4 supraglottic carcinomas, having a higher likelihood of local control after RT, can be identified based on primary tumor volume measurement on CT: tumors, 6 mL have a probability of 89% of local control with preservation of laryngeal function, while tumors .6 mL have only a control rate of 40%.[12,13] Another group[14] also reported a significant difference in local outcome after RT in supraglottic cancer based on tumor volume, with local control rates for tumors with volumes greater than or less than 8 mL being 20% and 70%, respectively (Figs. 206.11, 206.12, and 206.16).

In supraglottic cancer, the status of the neck frequently determines the preferred treatment for the primary lesion. Patients with a clinically negative neck but high risk for subclinical bilateral neck disease may be treated by RT because of the ease of bilateral elective neck irradiation.

After radiation of supraglottic cancer, laryngeal edema may persist for several months to a year. Anatomic distortions often persist both clinically and on images following successful irradiation, especially in the more advanced cancers (Chapter 157). Neck dissection increases the degree of lymphedema and fibrosis.

Combined RT and surgery as well as chemoradiation and surgery are common strategies in advanced cancers. T4 lesions generally receive postoperative irradiation. Radiation therapy is added for close or positive margins, invasion of soft tissues of the neck, subglottic extension, cartilage invasion, multiple positive lymph nodes, and extracapsular extension. Note that the last five of these factors can be obtained from diagnostic imaging prior to initiating any therapy.

Glottic and Subglottic Cancer

Since the goal of treatment is almost always cure, with the best functional result, while minimizing risk of a serious complication, early glottic cancer is usually treated initially by RT or transoral laser excision. Late glottic cancer can be treated with RT, holding laryngectomy in reserve for failure or with total laryngectomy possibly followed by RT. This decision making relies heavily on imaging findings. The balance between surgical and RT approaches for a laryngeal preservation strategy are discussed in detail in the prior section on surgical treatment.

Surveillance Options

Clinical follow-up is usually every 4 to 6 weeks for 2 years, every 3 months for the third year, and then every 6 months.

Clinically, it is common to suspect recurrence and obtain a negative biopsy at direct laryngoscopy. The odds of such disparate results are increased by persistent edema. Progressive or persistent symptoms will cause clinicians to desire repeat biopsies.

Surveillance imaging strategies should be aimed at detecting recurrence as early as possible and reducing unnecessary biopsies. These strategies must also take in account the risk of second head and neck primaries, lung cancer, and other cancers. Anatomic (CT and MR) and physiologic (FDG-PET) tools are available and should be used in clinically appropriate cases but not as a routine.

Recurrences almost always occur within 2 years. Recurrences after 5 years are rare and may be difficult to distinguish from a new primary tumor. Local recurrence increases the risk of metastatic disease in lymph nodes, and the lymph nodes should either be electively treated or watched very closely.

Recurrence after radiation therapy often presents as a return of hoarseness or persistence and especially worsening of lymphedema beyond 1 or 2 months post RT. Recurrent tumor may be entirely submucosal (Fig. 206.33). Generous, deep biopsies are required to confirm recurrence. Such biopsy technique can precipitate a laryngeal necrosis in a patient cured of cancer. A combination of FDG-PET and diagnostic-quality CT can be used to triage patients to biopsy. A negative FDG-PET is especially useful to exclude recurrence but must be done 2 to 3 months after completion of therapy to avoid false results.

Recurrence after surgery may be difficult to pick up early because the larynx is deformed following radiotherapy and/or partial laryngectomy or the disease is deep to the mucosa following total laryngectomy with reconstruction of the pharynx (Fig. 206.34 and Fig. 206.35). A baseline anatomic imaging study may be necessary to detect recurrence if FDG-PET or the clinical circumstances are not definitive. Total laryngectomy will salvage almost all failures confined to the larynx that are not suitable for an attempt at radiation salvage.

Radiation therapy alone will usually not cure a patient with recurrence in the neopharynx, neck or, stoma after total laryngectomy. Surgical resection should be considered for stoma recurrence. Imaging is critical in this decision making. The main contraindications to curative salvage surgery for stomal recurrence are extensive direct upper mediastinal invasion and encasement of the tracheal and/or brachiocephalic arteries. Neopharyngeal recurrence that is multifocal (Fig. 206.28) or deeply infiltrating to the floor of the neck or carotid cannot be salvaged. More limited neopharyngeal recurrence may be salvageable especially if surgery and RT can be used in combination (Fig. 206.30). Changes due to radionecrosis may mimic or coexist with recurrent cancer (Figs. 206.36–206.39). This is discussed in more detail in a following section Post Treatment Imaging Findings.

DISEASE ACUITY AND REPORTING RESPONSIBILITY

Laryngeal carcinoma usually is known or suspected at the time of imaging, so no special communication is required.

Some special circumstances arise that require immediate direct communication with the referring treatment provider. These include the following:

- Any time the tumor places the airway at risk (Fig. 206.15)
- When there might be superimposed infection
- When it may be anticipated from imaging that a tracheostomy might cross tumor (Fig. 206.23)
- In a post-RT patient where the larynx has become necrotic and may collapse and the patient has not had a tracheostomy (refer to the Posttreatment Imaging Findings section)
- If a tumor is discovered that was not clinically suspected

It is very important that the report contains a complete assessment of the disease extent and all information that is relevant to treatment planning. The nature of this information should be apparent from study of the prior sections on treatment options. This must include precise comments with regard to the following issues:

Primary Site Evaluation

- Extent of invasion along mucosal structures within the larynx and adjacent tongue base, hypopharynx, trachea, and esophagus
- Subglottic extent

- Spread to deep tissues spaces within the larynx, including the pre-epiglottic and paraglottic spaces
- Spread to the laryngeal skeleton–cartilage invasion
- Extralaryngeal spread to the deep neck

Perineurovascular Spread

- Involvement of the recurrent laryngeal or superior laryngeal neurovascular bundle
- Evaluation of regional lymph nodes emphasizing levels 2 through 6

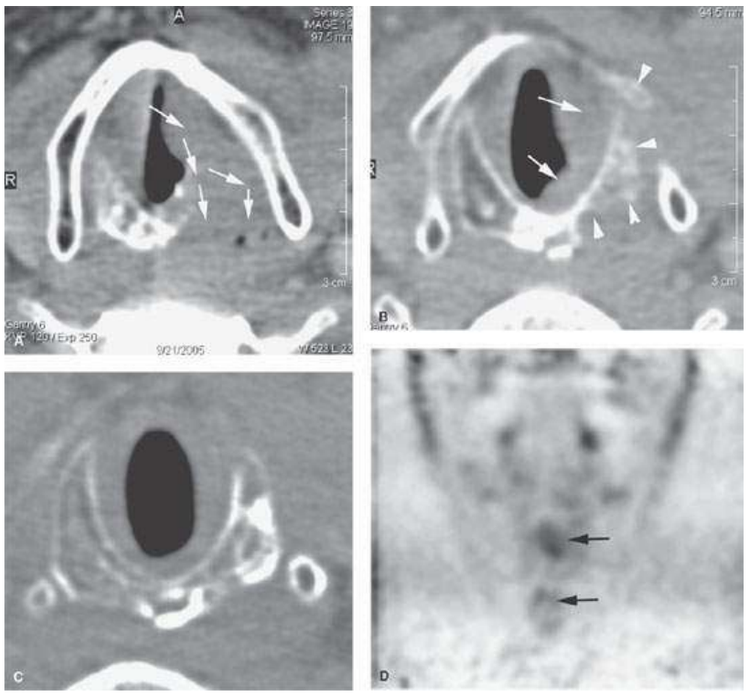


FIGURE 206.33. A patient treated with radiotherapy for laryngeal carcinoma. The contrast-enhanced computed tomography study done in follow-up shows anatomic evidence of recurrence. A: Tumor of the true cord infiltrating the paraglottic space and destroying the thyroid and arytenoid cartilages (arrows). B: Sections in the mid subglottis showing endoluminal tumor (arrows) and destruction of the thyroid and cricoid cartilages (arrowheads). C: Section in the low subglottis showing cricoid cartilage sclerosis related to involvement by tumor. (NOTE: All of this recurrent disease was submucosal. Fluorine-18 2-fluoro-2-deoxy-D-glucose positron emission tomography [FDG-PET] was done even though diagnosis of recurrence was virtually certain since no features of necrosis were present. D: FDG-PET showing several areas of hypermetabolic activity in the larynx (arrows). Total laryngectomy showed extensive recurrent tumor.)

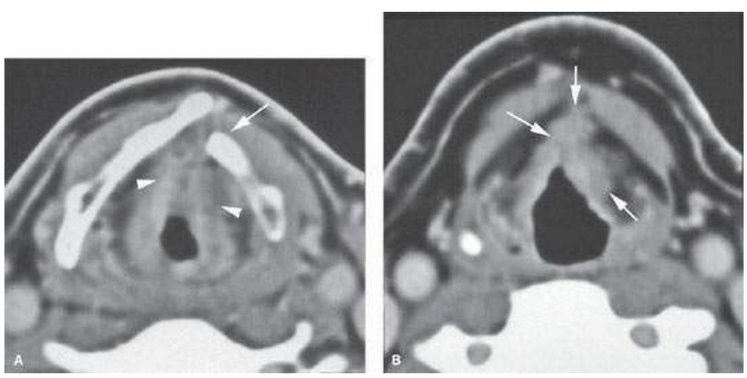


FIGURE 206.34. Contrast-enhanced computed tomography study of patient with pain several years after partial laryngectomy for vocal cord carcinoma. No baseline study was available. A: Deformity of the laryngeal skeleton (arrow) consistent with that seen in vertical hemilaryngectomy is present. Soft tissue changes at the level of the reconstructed vocal cords are nonspecific (arrowheads). B: While the soft tissue findings in (A) were not specific, those in this image show obviously infiltrating tumor in the pre-epiglottic space (arrows). The patient was salvaged with total laryngectomy, and extensive recurrent tumor was confirmed.

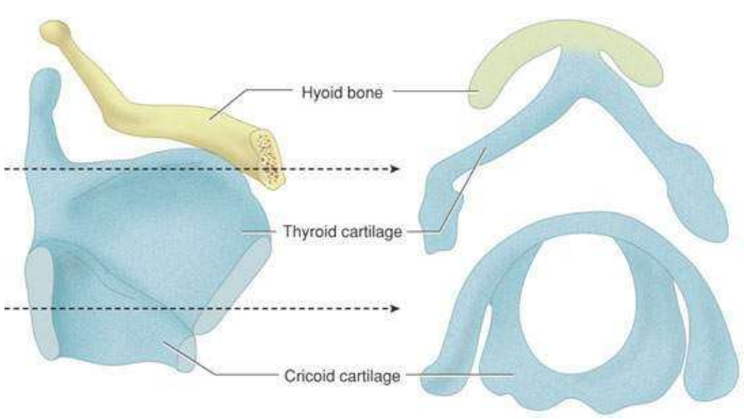


FIGURE 206.35. Diagram showing the effects of weakening of the laryngeal skeleton due to radiation effects. Such an appearance can also be seen if patients are studied with the neck in a flexed position. Such positioning during a laryngeal study should be avoided. Weakening of the membranes attaching the cartilage portions of the laryngeal skeleton causes the hyoid bone to collapse or telescope onto the thyroid cartilage and the thyroid cartilage could do the same to the cricoid. This sometimes results in unusual and potentially confusing axial images.

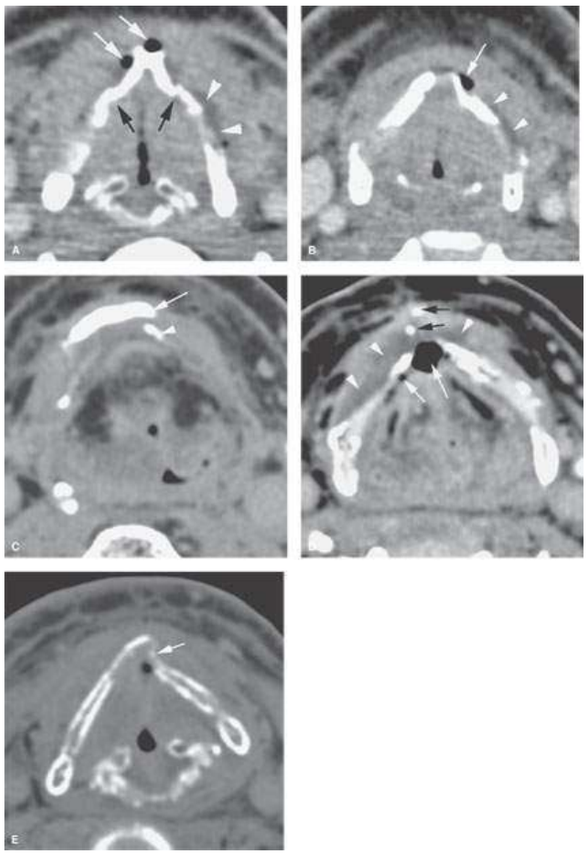


FIGURE 206.36. Two patients with radionecrosis shown on CECT studies. A, B: Patient 1, A: There is gas in the prelaryngeal soft tissues (white arrows) and edema or perhaps fluid between the strap muscles and the thyroid lamina (arrowheads) in that space. There is evidence of paramedian weakening and inward collapse of the thyroid lamina (black arrows). B: Section at the level of the false cords shows the gas (arrow) and fluid or edema (arrowheads). (Note: This is evidence of early laryngeal necrosis. There are no findings to suggest recurrent tumor. Once the larynx begins to buckle inward there is a risk of acute airway occlusion.) C–E: Patient 2 with the laryngeal necrosis more advanced than that of the Patient 1, C: The thyroid cartilage (arrowhead) and hyoid bone (arrow) are to close together. There is extensive swelling in the supraglottic larynx with possible airway compromise. D: There is an obviously large pocket of gas in the midline and smaller ones more laterally (white arrows). In addition, there is extensive edema or fluid collection outside the larynx (white arrowheads) and fragments of cartilage seen anteriorly (black arrows). E: In the same patient there is weakening and bowing (arrow) of the thyroid cartilage in the paramedian location carrying a risk of sudden collapse of the laryngeal skeleton. (Note: This patient had a tracheostomy soon after this study and was eventually salvaged with laryngectomy due to ongoing necrosis. No tumor was present in the specimen.)

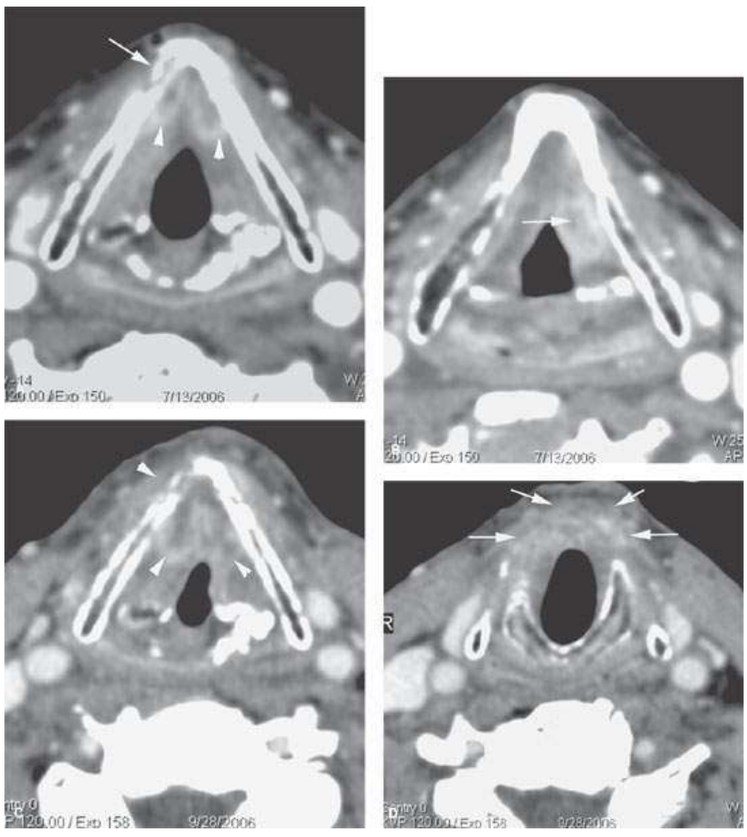


FIGURE 206.37. A patient treated with radiotherapy for glottic carcinoma. Two CECT studies two months apart were done because of the suspicion of recurrence. A: There is an enhancing mass at the anterior commissure (arrowheads) and early fragmentation of the thyroid cartilage (arrow). B: At the false cord level there is focal thickening in the paraglottic space a finding that must be considered for suspicious for persistent tumor. (Note: At this point it was uncertain whether the changes seen here were due to necrosis or radionecrosis coexistent with recurrent tumor.) C: The second study showed a progressive mass at the anterior commissure and progressive fragmentation of the thyroid lamina especially on the right (arrowheads). D: A section through the upper subglottis showed a fairly diffuse slightly enhancing mass growing in the prelaryngeal soft tissues and infrahyoid strap muscles (arrows). (Note: This rapid progression was considered extremely suspicious for tumor coexistent with necrosis. Patient had a total laryngectomy and tumor recurrence was confirmed.)

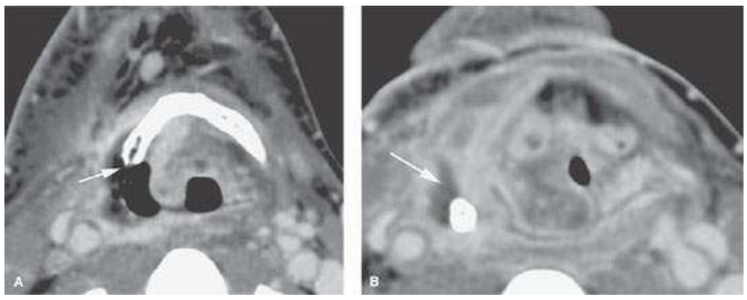


FIGURE 206.38. Patient treated with radiotherapy for a marginal supraglottic primary tumor. CECT study was done because of pain following therapy. A: There is a large gas and fluid filled cavity (arrow) surrounding the necrotic hyoid bone. B: This process continued all the way down the thyroid lamina mainly outside the larynx to surround the superior cornu of the thyroid cartilage (arrow) which articulates with the hyoid bone and a similar cavity filled with fluid, air and surrounded by extensive enhancing tissue was present. There was also significant laryngeal edema present. (Note: At this point, necrosis alone cannot be differentiated from necrosis with tumor. FDG PET would be unlikely to help in this circumstance since would almost certainly show the process to by hypermetabolic. The patient eventually came to laryngectomy. Only necrosis was found. The laryngectomy was done because the larynx had no functional use and the patient was in pain and aspirating.)

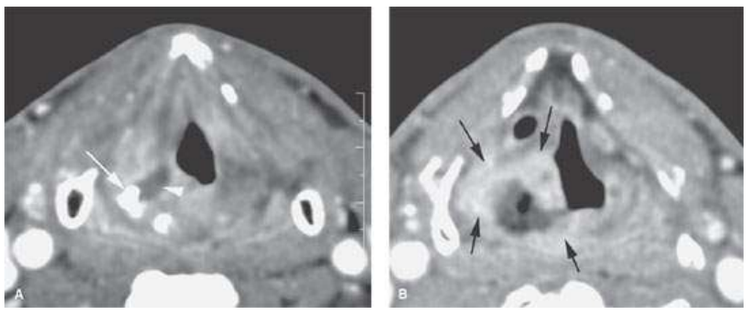


FIGURE 206.39. A patient treated with radiotherapy for marginal supraglottic carcinoma. The patient had pain and dysphagia. CECT was done. A: Shows a sclerotic arytenoid (arrow) surrounded by a small fluid filled cavity an appearance consistent with localized arytenoid necrosis. However, more extensive disease was seen superiorly. B: Shows a necrotic appearing mass of the aryepiglottic fold containing fluid and debris and gas. There was surrounding enhancing mass (arrows). At this point one cannot be certain whether this represents an extensive arytenoid necrosis or coexistent necrosis and tumor. A period of conservative management failed to produce any resolution. Biopsy revealed recurrent tumor. (Note: In this case the extent of the soft tissue changes is more than that usually seen in a simple arytenoid necrosis but that was still a distinct possibility and such changes can resolve and the larynx heal. These cases require close surveillance since when a mass is this extensive recurrent tumor becomes much more possible. FDG PET in these situations usually is not helpful since the radiolnuclide study is hypermetabolic in both the reactive usually infected processes as well as in recurrent tumor. A negative FDG PET would support necrosis.)

OTHER MALIGNANT LARYNGEAL TUMORS

Etiology

Other malignant laryngeal tumors are rare and have no specific etiology.

Prevalence and Epidemiology

These are rare sporadic malignancies. The nonchondroid sarcomas tend to occur in children and younger adults. Chondrosarcoma is the most common of these rare lesions. The epithelial lesions are very rare in the pediatric age range.

Clinical Presentation

More common presentations are the same as those of laryngeal SCCA. There will be an indication of vocal cord dysfunction, pain in the larynx perhaps with elements of dysphagia, and throat or referred ear pain. These tumors occasionally present as a neck mass; however, unlike SCCA, they usually are due to the primary rather than related adenopathy. These circumstances then lead to discovery of a submucosal mass in the larynx at endoscopy. Endoscopy may also show a mucosal lesion that looks like SCCA but is eventually proven to be one of these rare tumors histologically.

Pathophysiology and Patterns of Disease

Benign and malignant minor salivary gland tumors (Fig. 206.40) arise from the mucous glands deep to the laryngeal mucosa and tend to remain submucosal as they grow. These tumors are rare. Even more rarely, a carcinoid, lymphoma (Fig. 206.41), plasmacytoma (Fig. 206.42), neurogenic tumors including small cell carcinoma (Fig. 206.43), and mesenchymal sarcoma (Figs. 205.9 and 206.44) will arise in the larynx and/or pharynx. Enchondroma and osteochondroma and chondrosarcoma (Fig. 206.45) of the laryngeal skeleton are also rare but are generally the most common of this group of rare lesions. Since these “noncarcinoma” cancers will typically arise from submucosal structures, their growth tends to remain primarily submucosal and their site of origin from the hypopharynx or larynx may not be entirely clear at endoscopy. The chondroid tumors are most often benign or low-grade malignancies. Sarcomas can also arise from other elements of the laryngeal skeleton and closely related infrahyoid strap muscles. The rare instances of metastases to this region are usually supraglottic (Fig. 206.46).

The spread patterns of these tumors are generally not distinguishable from those of SCCA described in the previous section. Some will enhance more than the average SCCA, but this is not a truly distinguishing characteristic.

Chondrosarcomas arise from the cricoid and much less frequently the thyroid cartilages (Fig. 206.40). These tumors may express an ossified chondroid matrix.

Lymphoma (Fig. 206.41) may be more diffusely infiltrative and mimic diseases such as amyloidosis, sarcoidosis, and Wegener granulomatosis discussed in Chapter 204. Posttransplantation lymphoproliferative disorder may affect the head and neck; it is most commonly seen in the Waldeyer ring but may be localized in the supraglottis.

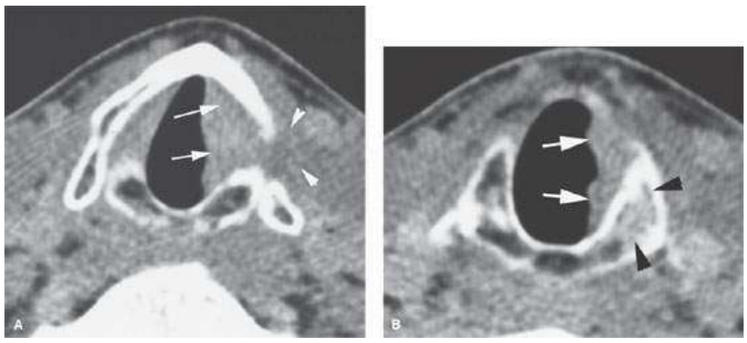


FIGURE 206.40. CECT study in a patient with true vocal cord dysfunction due to an adenoidcystic carcinoma of the larynx growing without any mucosal component. A: Tumor grows on the under surface of the true vocal cord (arrows) and into the soft tissues of the neck (arrowheads). B: Subglottic spread (arrows) with reactive changes of the adjacent cricoid cartilage (arrowheads) is present.

Manifestations and Findings

Computed Tomography and Magnetic Resonance Imaging

CT and MRI will show infiltrating lesions involving the mucosal structures and deep planes in and around the larynx described in the patterns of spread section for SCCA. Cartilage invasion is manifest and evaluated in a manner also described in those sections and in the sections on controversies.

The areas of infiltrating tumor will usually enhance more than muscle, perhaps quite a bit more. They replace fat and may spread along neurovascular bundles or natural areas of weakness in the laryngeal skeleton and other pharyngeal walls. The details of how these mucosal and nonmucosal lesions spread and tend to appear on CT and MRI are discussed with general tumor growth patterns (Chapters 21 and 23) and then the respective chapters in Section II that consider those specific lesions.

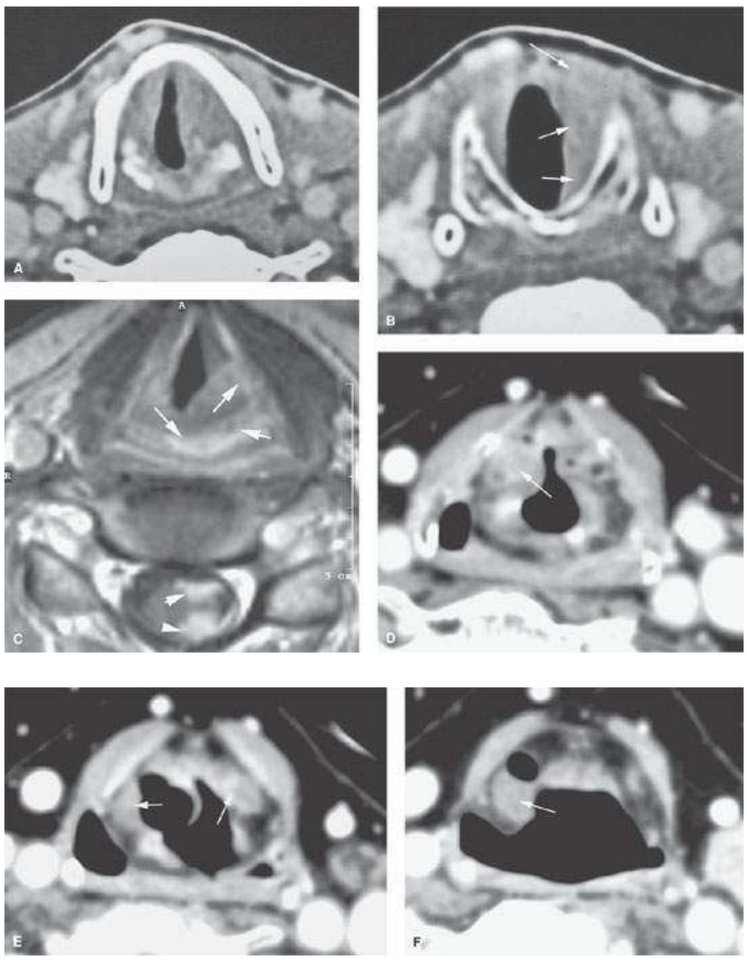


FIGURE 206.41. Three patients with laryngeal lymphoma A, B: In Patient 1 the lymphoma is confined to the glottic and subglottic levels and is indistinguishable from SCCa. C: MRI of Patient 2 with CNS disseminated non Hodgkin's lymphoma the CE T1W image correlating showing pia-arachnoid "caking" of the spinal cord (arrowheads) and spread to the arytenoid pad of the posterior laryngeal wall (arrows). D–F: Patient 3 had predominantly multifocal (arrows) supraglottic disease with involvement of the false cord and aryepiglottic folds. (continued)

Ultrasound

There is no role for ultrasound in these unusual lesions.

Nuclear Medicine

There is no routine role for radionuclide studies in these unusual lesions since their metabolic behavior on FDG-PET studies is unpredictable.

Catheter Angiography

Rarely, a hypervascular mass such as a paraganglioma may be called into question based on imaging findings. If so, catheter angiography may be required for diagnosis and perhaps as an aid to endovascular adjunctive therapy.

Endoscopy

Endoscopy will often show these lesions to be entirely submucosal. Otherwise, the diagnosis is usually a "surprise" following review of the material obtain for pathologic evaluation.

Differential Diagnosis

From Clinical Data

The differential diagnosis is usually SCCA in mucosally obvious primary tumors. In submucosal lesions, the differential of an entirely submucosal SCCA is still possible. Multiple lesions suggest a rare case of metastatic disease to the larynx (Fig. 206.46). Otherwise, laryngocele (Chapter 203) and the very rare submucosal benign tumor (Chapter 205) are the most likely considerations. An inflammatory lesion of the laryngeal skeleton or mucosal or submucosal tissues can mimic these malignancies as SCCA. Chondritis can mimic chondrosarcoma (Fig. 205.7).

Tuberculosis, syphilis, and other infections can rarely mimic cancer, as discussed in Chapter 204. Infection is usually not anticipated, with the nature of the disease being revealed at biopsy.

Posttransplant lymphoproliferative disorder may affect the larynx, but the clinical situation should make that diagnosis relatively obvious.

From Supportive Diagnostic Techniques

The differential diagnosis is usually that of a submucosal mass that will most of the time turn out to be SCCA. Otherwise, the differential based on laboratory or other unusual clinical circumstances is the same as discussed in the previous section on hypopharyngeal SCCA. Multiple lesions seen on imaging studies suggest a rare case of metastatic disease to the larynx (Fig. 206.46) and multifocal infiltrating patterns suggest lymphoma.

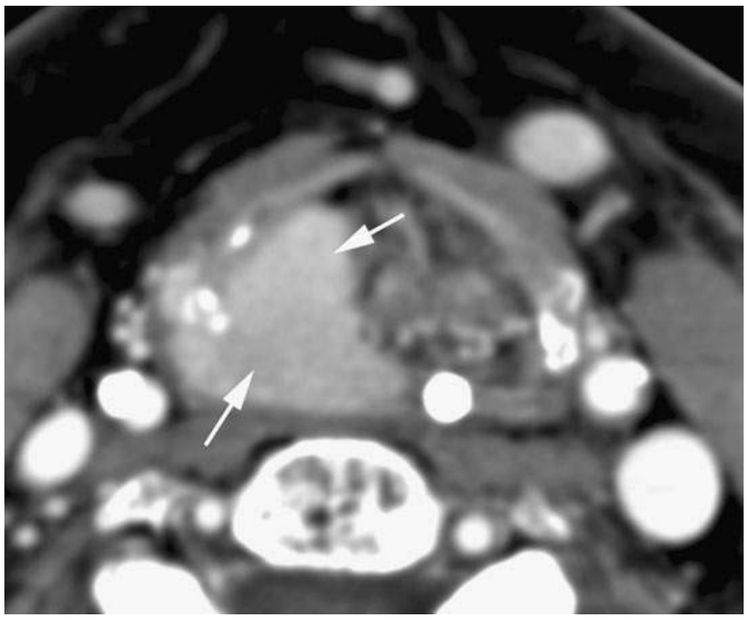


FIGURE 206.42. CECT of a patient with extramedullary plasmacytoma of the larynx (arrows).

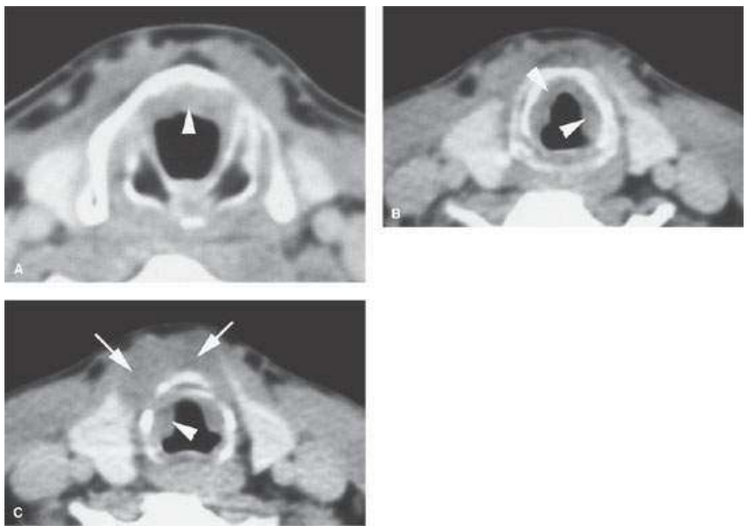


FIGURE 206.43. CECT of a patient presenting with hoarseness and a very unusual infiltrating pattern of tumor within the larynx. A: A broad zone of soft tissue thickening (arrowhead) noted in the upper subglottis. B: Lobulated lower subglottic soft tissue thickening (arrowhead). C: Lobulated thickening near the junction of the cricoid and trachea this level being at the first tracheal ring. Also considerable amount of tumor infiltrating anterior to the trachea (arrows). (Note: This very unusual spread pattern being cricotracheal with a large component in the soft tissues raised the possibilities of a lesion other than squamous cell carcinoma. Biopsy returned small cell (neuroendocrine) carcinoma.)

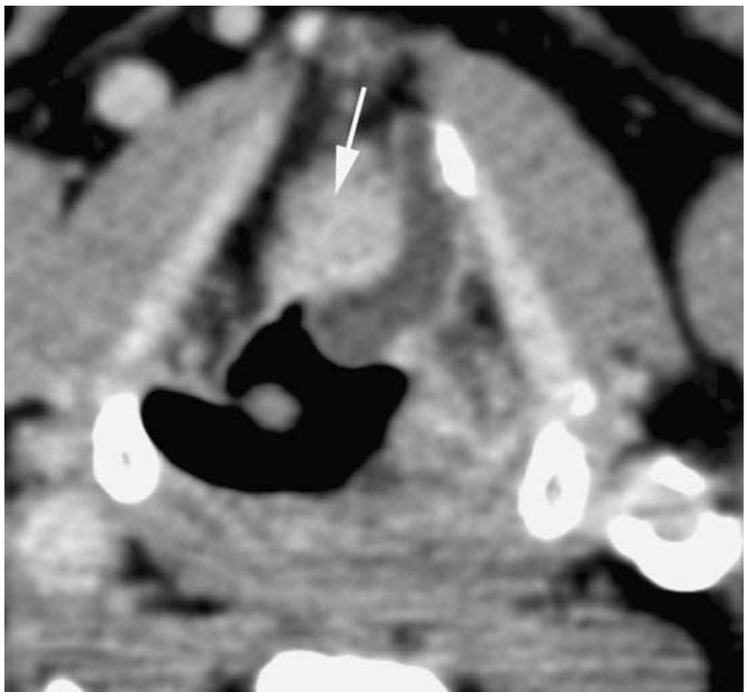


FIGURE 206.44. CECT of a patient presenting with vocal cord dysfunction and a large submucosal mass, mainly due to a laryngocele (other images in Figure 203.3) caused by this obstructing leiomyosarcoma (arrow).

Medical Decision Making and Treatment Options

Medical

Chemotherapy may play an adjunctive or primary therapeutic role, such as in lymphoma.

Surgical

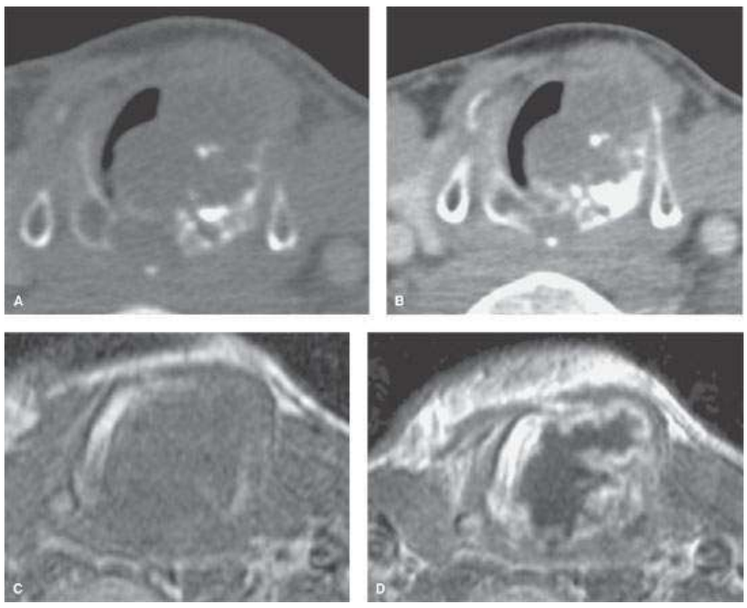
Surgical decision making is based on histology and then the same principles outlined for hypopharyngeal-origin SCCA.

Radiotherapy

RT decision making is based on histology and then the same principles outlined for SCCA.

Surveillance Options

The follow-up policy will vary based on the histology of the tumor, its biologic aggressiveness, and chosen therapy. Almost all have at least one baseline CT or MRI at 3 to 6 months after the completion of treatment and another at 1 year. Additional need for follow-up examination is then individualized. The role of FDG-PET in these patients would be difficult to generalize but certainly would depend on histology at least in part.



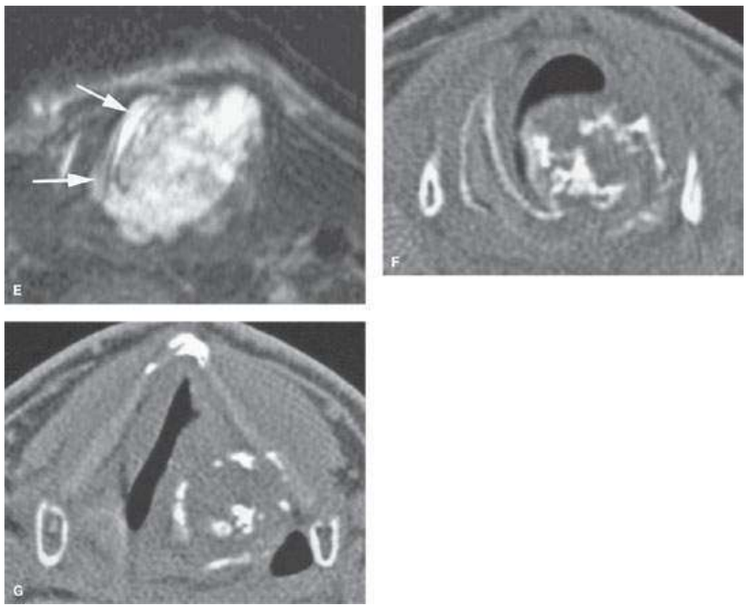


FIGURE 206.45. Two patients with laryngeal chondrosarcoma. A–E: Patient 1. CT and MR images of the chondrosarcoma arising from the cricoid cartilage. A, B: Bone and soft tissue views respectively showing the extent of the soft tissue mass and matrix calcification involving predominantly the left side of the cricoid cartilage. C: T1W non contrast image showing the tumor matrix to be lower in signal intensity than muscle. D: CE T1W image showing predominately peripheral enhancement of the tumor and a large central portion that is non-enhancing. E: T2W image somewhat degraded by motion artifact showing the tumor to be of generally bright signal intensity so that it cannot be differentiated from the fat within the normal right cricoid arch (arrows). F, G: Patient 2 CT study showing a laryngeal chondrosarcoma with a more typically calcified chondroid matrix than in Patient 1 extending the aryepiglottic fold in (G).

DISEASE ACUITY AND REPORTING RESPONSIBILITY

These lesions are treated the same as SCCA. Please reference that previous discussion in this chapter. If atypical features are noted on the imaging studies, this might lead to anticipation of an unusual histology prior to biopsy and the endoscopist may forewarn the pathologist that this is possible.

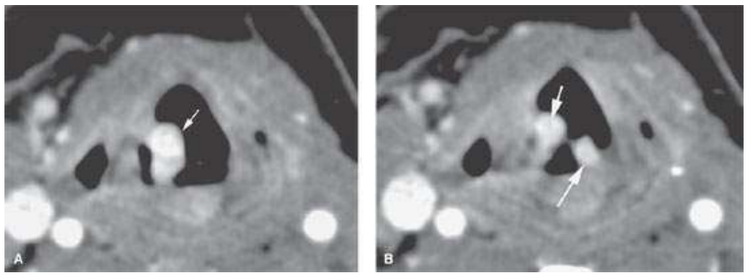


FIGURE 206.46. CECT showing multiple thyroid metastases to the supraglottic larynx (arrows).

POSTTREATMENT IMAGING FINDINGS

Posttreatment Complications: Clinical Perspective

The postoperative complications important for imaging include the deformity of open partial laryngectomy and perhaps webs.

The most common late complication of RT is edema of the larynx. The rate of edema resolution is related to the dose of radiation, volume of tissue irradiated, addition of a neck dissection, continued use of alcohol and tobacco, and size and extent of the original lesion. Clinical edema may take as long as 6 to 12 months to resolve when there has been both RT and neck dissection.

Soft tissue necrosis leading to chondritis and chondronecrosis occurs in, 1% of patients. Soft tissue and cartilage necroses mimic recurrence. Clinically, these patients experience hoarseness, pain, and edema; a laryngectomy may be recommended in desperation for fear of recurrent cancer. Imaging can vastly alter the course of this clinical dilemma as noted in the following discussion.

Posttreatment Anatomic Imaging of the Larynx

CT and/or MR are the follow-up anatomic imaging modalities used to study patients irradiated for laryngeal cancer. CT is preferred because of its higher resolution; depiction of cartilage patterns of change suggestive of necrosis; and ability to detect gas and fluid, which are potentially differentiating features of osteoradionecrosis of the laryngeal skeleton (Figs. 206.35–206.39). The first skill necessary in anatomic surveillance is an understanding of expected posttreatment changes discussed in Chapter 21 (Figs. 21.68 and 21.69). One must absolutely not definitively diagnose normal postirradiation changes as recurrent tumor. Such interpretations could lead to unnecessary deep biopsies that progress to chondronecrosis and eventually an unnecessary laryngectomy.

Imaging reveals consistent and obvious postirradiation changes in the larynx at doses .6,500 cGy. Mucositis will be seen as superficial, increased signal on T2-weighted MR, and excessive contrast enhancement on CT. This is most apparent during and for 6 weeks to 3 months following therapy. Increased mucosal signal on T2-weighted MR may persist for many more months or years. Laryngeal soft tissues characteristically look “boggy” or thickened compared to normal (Fig. 21.69). This swollen appearance is at its maximum from the end of therapy to about 3 months following completion of therapy. The edema involutes, but secondary perilymphatic fibrosis causes the swollen appearance to persist indefinitely. Persistent, stable thickening of the free margin of the epiglottis, aryepiglottic folds, FVCs, posterior walls of the larynx, and pharyngeal wall is essentially permanent after high-dose RT. This increased thickness is accompanied by vague increased density in the fat of the pre-epiglottic space and paraglottic space as well as the fat within the aryepiglottic folds up to 3 to 12 months following completion of therapy. After 3 to 12 months, the fat planes become more distinct. A vague, increased density may remain visible within the deep fat spaces, probably representing perilymphatic and other fibrosis within this fibroadipose connective tissue. The intrinsic laryngeal musculature may become atrophic and the fat partially replaced. This muscular finding is most common on the side of a fixed TVC that does not become mobile following treatment. This atrophy is one possible reason for lack of return of normal function in a successfully treated patient. The subglottic larynx will often show persistent thickening of the mucosa adjacent to the cricoid perichondrium (Fig. 21.69G). This appearance of circumferential subglottic thickening is not “normal” in the untreated larynx. MRI is no more specific than CT in its rendering of these changes, except that T2-weighted images will reveal edematous mucosa and fat by virtue of its increased water content and high signal.

The primary tumor mass gradually involutes during successful RT. An obvious focal mass can persist up to 3 months or more following successful therapy. Residual focal abnormalities are more common on the side of a lateralized lesion and in originally larger-volume lesions. It is best to avoid imaging until 3 months after the completion of therapy so that one is not tempted to biopsy the limited areas of CT or MR abnormality. Slight asymmetry is the rule in larger or lateralized lesions, and such findings can persist indefinitely. Focal, fairly discreet abnormalities about $1 cm persisting beyond 3 months should be carefully observed clinically, including supplemental imaging. Such minimal residua usually turn out to be sterilized posttreatment fibrosis that remains stable over many years; however, they can be the earliest sign of persistent tumor (Fig. 206.42B). Stable persistent anatomic imaging findings on three consecutive imaging studies done at 3- to 4-month intervals virtually never are due to recurrent or persistent tumor.

Imaging surveillance should be reserved for patients who are either at high risk for failure and/or those who are suspected clinically of failure. By comparing subsequent studies with the baseline study, it becomes possible to detect tumor recurrences with more confidence. In one study,15 tumor recurrence was detected on surveillance imaging in 40% of cases at an earlier time point than with clinical follow-up alone.

The patient having either surgery alone or combined treatment may also benefit from follow-up imaging. Conservation laryngeal operations make this task difficult since the deformity of the larynx produced by the surgical procedure disturbs the symmetry that is so useful for image interpretation. Deep tissue planes such as the paraglottic and pre-epiglottic spaces are usually significantly altered and sometimes scarred (Fig. 206.34). Baseline studies should be done in high-risk patients about 3 months postoperatively.

Following total laryngectomy or laryngopharyngectomy, baseline studies are usually not necessary since the reconstructed neopharynx and peristomal region are relatively easy to evaluate (Fig. 206.32). If recurrence develops at the stoma, the stomal site and mediastinum must be studied in detail to determine the level of tracheal involvement, possible spread to the muscular wall of the esophagus, encasement of the aorta and brachiocephalic vessels, mediastinal adenopathy, and pulmonary metastatic disease. MR is particularly useful for showing tracheal invasion, spread to the muscular wall of the esophagus, paravertebral or prevertebral muscle invasion, and vascular encasement but not mediastinal and hilar adenopathy. CT is better for detecting nodal disease and pulmonary metastases.

Posttreatment Physiologic Imaging of the Larynx

After 3 months, a negative FDG-PET study can exclude persistent disease with a high degree of confidence. A positive FDG-PET has about a 25% chance of being falsely positive but certainly is worrisome.

Some practices recommend FDG-PET as the initial baseline study, in patients treated with advanced disease with low clinical suspicion of recurrence, and in patients with nonspecific symptoms that could indicate recurrence but without a clinically obvious mass; cross-sectional imaging should then be performed for an equivocal or positive PET study, or as the initial study in patients with a suspicious palpable mass or recurrent tumor confirmed by biopsy.16 Further study is needed to elucidate the most efficient use of PET and CT/MR in posttreatment situations.

In surveillance, FDG-PET has the advantage of detecting metastases as well as second primaries in the lung and elsewhere. It also carries the burden of frequent false-positive activity throughout the upper pharynx, especially at the tongue base and tonsils. Obviously, large or progressively enlarging masses are another matter and usually indicate recurrent tumor.

If there is an indeterminate clinical mucosal lesion or focal mass on an anatomic CT or MR image, the use of FDG-PET might lead to earlier rather than later biopsy confirmation.

Diagnostic Imaging in Laryngeal Osteonecrosis and Chondronecrosis

Radiation-induced laryngeal osteonecrosis and chondronecrosis is an uncommon complication of RT. It is often impossible to tell if one is dealing with such tissue necrosis alone or in combination with recurrence, either clinically or with imaging studies. Moreover, the two situations may coexist.

Perichondritis and chondronecrosis manifest first by soft tissue swelling on CT or MRI. The findings of these processes are easier to recognize on CT than MRI because of the better CT images of cartilage detail and easier recognition of small gas collections adjacent to the laryngeal skeleton; these collections may be either in the paraglottic space and/or between the cartilages and infrahyoid strap muscles (Fig. 206.43A,B).

The findings may be focal if only the arytenoid is involved (Fig. 206.44) or more diffuse when both thyroid laminae are involved (Fig. 206.43D,E). The inflammatory swelling will usually be found adjacent to the area of eventual cartilage necrosis. This may be a very subtle change as it lies between the strap muscles and thyroid cartilage, an unusual place for more “routine” post-CT edema. Deep ulcerations containing gas or complete loss of tissue are more advanced soft tissue findings that frequently herald cartilaginous involvement. The inflamed soft tissues will enhance with intravenous contrast, and pockets of fluid or abscesslike cavities are frequently visible within or next to dead and dying cartilage and bone (Fig. 206.45).

The affected cartilage(s) often become sclerotic. This mimics the progress of osteonecrosis in irradiated bone elsewhere in the body. As the cartilages weaken, the laryngeal skeleton may begin to collapse. The cricothyroid and thyrohyoid membrane and ligaments shorten with contractures. The thyroid laminae will bow inward when weakened, and this bowing may be the earliest sign of weakening. This bowed inward pattern is especially common if the tumor was originally located at the anterior commissure (Figs. 206.43). In general, gross necrosis of the cartilage tends to occur at points of invasion by tumor, whether recognized or not, prior to RT. Late findings include fragmentation and sloughing of necrotic bone or cartilage leaving obvious defects (Figs. 206.42–206.45). The entire larynx may collapse, and fragments or osteomyelitic sequestra may lie within areas of dying soft tissue and cartilage. Some cases may heal without serious impairment of the larynx. Advanced cases may require laryngectomy, especially when there is a concern that coexistent recurrent tumor may be present.

When early signs of chondronecrosis become apparent on CT or MRI, the patients should be followed with imaging. Once weakening of the laryngeal framework is noted, one should strongly consider controlling the airway via tracheostomy. This weakening manifests mainly as inward bowing or inward fragmentation and collapse of the thyroid cartilage (Fig. 206.43). Sudden death, possibly simply induced by coughing, has occurred in the face of such imaging findings and failure to prophylactically control the airway.

What the Treating Physician Needs to Know
The treating physician needs to know the following:

- If not SCCA, then the likely alternative diagnosis based on imaging
- Exact extent of the primary tumor lesion within the laryngeal soft tissues
- Evidence for invasion of the laryngeal framework and its extent, when present
- Evidence for extralaryngeal tumor extension and its extent when present
- Tumor volume
- With regard to the neck lymph nodes, their level of involvement, the location of pathologic lymph nodes, and if there is any evidence for extranodal tumor spread
- With regard to posttreatment imaging, suspicion for tumor recurrence, suspicion of radionecrosis, and risk for laryngeal collapse

Suggested Readings

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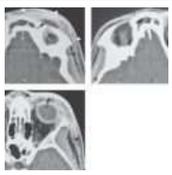
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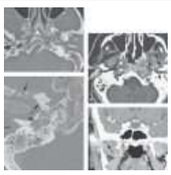
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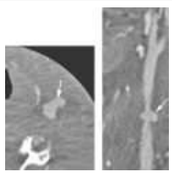
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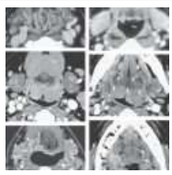
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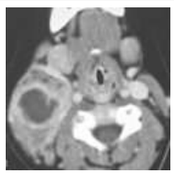
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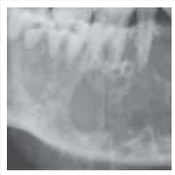
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