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Comparison of preoperative computed tomographic findings with postoperative histopathological findings in laryngeal cancers

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Abstract In this study of 22 patients with laryngeal cancer, computed tomographic (CT) scans in the axial plane were compared with histopathological sections prepared in the same plane. The value of the preoperative CT for evaluating tumor invasion, location and size was then investigated. Findings demonstrated that CT was most sensitive in determining tumor invasion to the paralaryngeal and pre-epiglottic spaces, anterior and posterior commissures and subglottis. In contrast, CT was less sensitive in determining actual tumor invasion to the laryngeal cartilages, extralaryngeal tissues and metastases to cervical lymph nodes.

Key words Laryngeal cancer · Computed tomography · Diagnostic studies

Introduction

Functional laryngeal surgery has become a popular technique for the treatment of laryngeal cancer. However, defining tumor extension between laryngeal mucosal surfaces and its cartilaginous framework and invasion to the extralaryngeal tissue planes is most important for classification of a lesion and for decision-making about treatment choice.

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Since only mucosal surfaces are seen during direct laryngoscopy, tumor invasion deep to the mucosa and surrounding cartilage, as well as affecting the ventricles and subglottis, cannot be determined sufficiently [3, 21]. However, while laryngeal mucosal surfaces, the laryngeal airway and laryngeal dysfunction can be determined by conventional radiological techniques, these techniques fail to show tumor infiltration into the paralaryngeal space (PLS) and pre-epiglottic space (PES) or extralaryngeal tumor spread [12, 18].

It has been widely accepted that computed tomographic (CT) scans in the axial plane are most useful for defining the extent and invasion of laryngeal cancer. The capability for evaluating deep laryngeal compartments, submucosal tissues, laryngeal cartilages and lymph nodes makes CT a valuable diagnostic technique in evaluating patients with laryngeal carcinomas preoperatively [1, 9, 17, 23, 27].

Materials and methods

Twenty-two laryngeal cancer patients (21 male, 1 female) were selected for this study. The mean age of the men was 57 and that of the woman was 60. All patients underwent microlaryngoscopy, during which the exact size, location and possible tissue invasion by tumor are defined and illustrated on an artist's drawing of the larynx.

CT was performed using a third-generation Siemens Somatom DRH CT scanner with the following technical factors: 5-s scan time, 125 kVp, 310 mAs, a window width of 350–500 HU. The patient was placed in a supine position with the neck hyperextended. The area between the base of the tongue and the first tracheal ring was determined for scanning on the lateral projection view. Scans were obtained using 4-mm-thick axial sections. In selected cases, such as glottic tumors, 2-mm sections were obtained for further definition of the lesion present. Intravenous contrast material (iopromide 763 ml/mg) was administered as a 100-ml bolus infusion just before scanning to facilitate detection of metastatic lymph nodes in the neck. Laryngeal cartilages were used as landmarks for evaluating CT images obtained.

All patients underwent laryngectomies, after which gross laryngectomy specimens were inspected with the naked eye. Specimens were then cut axially in 6 to 8-mm-thick sections. Tissues were fixed in 10% buffered formalin for 48 h. Decalcification was achieved in 10% buffered formic acid solution for approximately

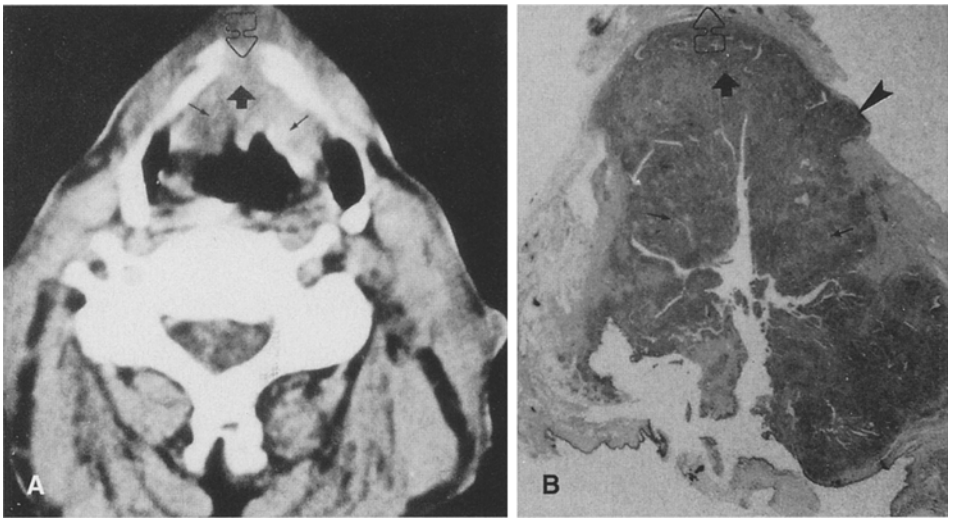

Fig. 1 **A** CT scan at the level of the ventricular bands. Bulky tumor infiltrates both ventricular bands and extends from the laryngeal surface of the epiglottis to the laryngeal vestibule. At this level, tumor infiltration into the paralaryngeal space (PLS, *short arrows*) and pre-epiglottic space (PES, *large arrow*) and thyroid cartilage destruction (*open arrow*) are clearly seen. **B** Histopathological specimen at the same level as the CT scan. Besides destruction of the thyroid cartilage, extralaryngeal tumor spread (*arrowhead*) is obvious

7–10 days. Specimens were next immersed in 70% alcohol, and embedded in a paraffin block for routine processing. Repeat microtome sections of 5–6 (m thickness were made until pathological slides corresponding to the CT sections were obtained. These sections were mounted on glass slides that had previously been thinly coated with albumin-glycerin. Finally, all slices were stained with hematoxylin-eosin.

Horizontal slides of histopathology corresponding to the CT sections were selected and compared with CT scans. The horizontal extent and growth pattern of each tumor were evaluated by both macroscopic and microscopic examinations.

Results

Histological examinations of the biopsy materials revealed squamous cell carcinoma in all 22 patients. Primary laryngeal carcinomas comprised 8 supraglottic, 5 transglottic, 1 subglottic and 8 glottic tumors.

Preoperative CT evaluations for tumor invasion of the PLS were evaluated in 17 patients. Findings were confirmed on histopathological examination in 14 of the cases, while 3 CT evaluations were false-positive (Fig. 1). One of the false-positive studies was related to the presence of inflammation and was misdiagnosed as tumor extension. Scans showed probable tumor invasion of the PES in 13 patients and these findings were confirmed on histopathology (Figs. 1, 2).

Gross cartilaginous destruction in 4 patients was correctly identified by CT, while in 2 patients microscopic foci of cartilage destruction were undetected. In 11 patients, there was a good correlation between CT and histopathological findings in demonstrating absence of tumor in cartilage. The accuracy rate for evaluating the thyroid cartilage was 68% (Fig. 1), while the false-negative rate was 9% (Fig. 2) and that for false-positives was 23%.

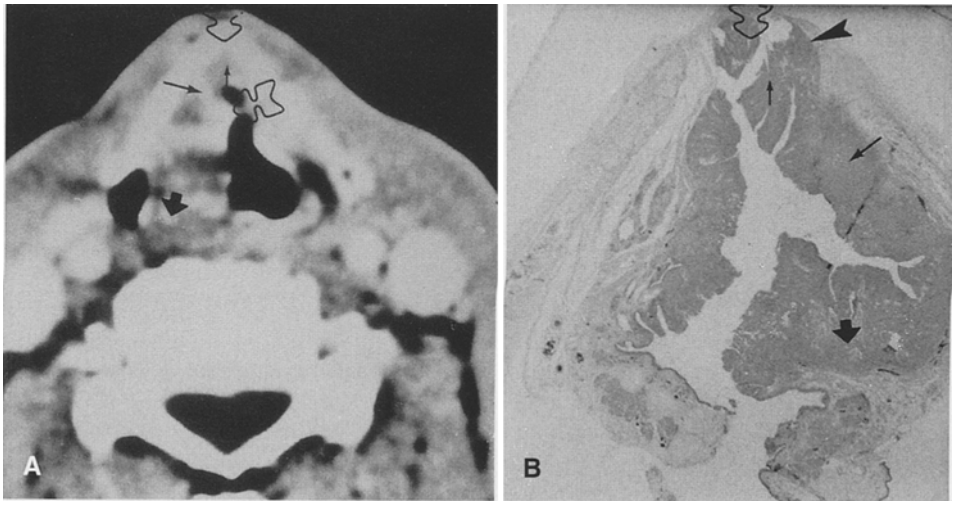

Fig. 2 **A** CT scan at the level of the ventricular bands. The mucosa of both ventricular bands is irregular. Tumor infiltration into the right PLS has caused increased bulk of the right ventricular band, while the right rima vestibuli is narrowed by bulky tumor (*large open arrow*). Tumor infiltration into the PES (*smaller open arrow*) and right PLS (*long arrow*) is clearly demonstrated. There is no cartilage invasion, but the lesion extends to the posterior commissure and narrows the right piriform sinus (*large arrow*). **B** Histopathological specimen at the same level as the CT scan. In addition to the scan findings, microscopic examination shows that tumor has resulted in destruction of the anterior thyroid cartilage and infiltrated into extralaryngeal tissues (*arrowhead*)

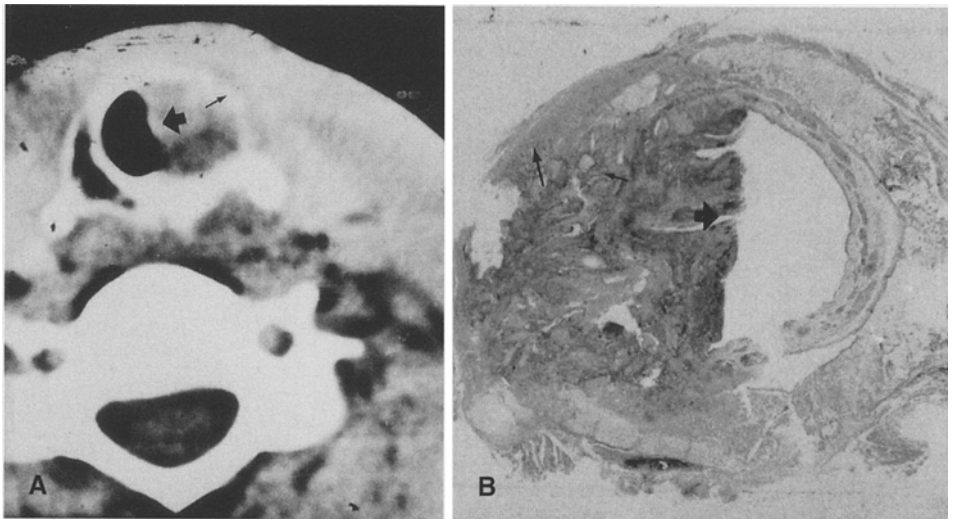

Fig. 3 Act scan obtained through the level of the inferior cornu of the thyroid cartilage. At the high subglottic level tumor mass involves the left half of the airway *(large arrow)*, while the left side of the cricoid cartilage is destroyed by tumor (*small arrow*). **B** Tissue section from the same level as the CT scan. In addition to the CT findings, tumor destruction of the cricoid cartilage can be seen. Extralaryngeal tumor infiltration (*long arrow*) is also easily seen

In contrast, histopathological sections revealed that the CT findings were false-positive in 5 patients. Of these 5 cases, 4 were "true" false-positive and 1 was evaluated as "normal", although tumor in this latter case was found adjacent to the inner surface of the thyroid cartilage.

Tomographic examination revealed that there was cricoid cartilage destruction in only 1 patient and this finding was confirmed on histopathological examination (Fig. 3).

In evaluation of epiglottic cartilage by CT, there was an excellent correlation demonstrating absence of tumor in 16 patients and invasion of the epiglottis in 2 patients. Tumor invasion into the epiglottic cartilage was suspected in 4 other patients, with histopathological sections corresponding to the scans showing the presence of epiglottic cartilage invasion in 3 patients, while 1 was found to be normal (Fig. 4).

CT scans showed tumor infiltration into the anterior commissure in 13 patients and these findings were confirmed on histopathological examination. In 2 cases CT was inadequate with regard to being able to define tumor invasion into the other vocal cord by crossing the anterior commissure (9%). Tumor invasion into the other vocal cord was identified as false-positive by CT in 1 patient, making the total accuracy rate for evaluating the anterior commissure 86% (Fig. 5).

A good correlation was found between CT and histopathology in determining tumor involvement of the posterior commissure in 9 cases (Fig. 5). However, in 2 other cases CT underestimated tumor crossover from one side of the commissure to the other. The overall accuracy rate of CT for evaluating the posterior commissure was 91%.

The presence of subglottic tumor extension was found on CT in 13 cases and was confirmed histopathologically in all of these cases (Fig. 3).

Extralaryngeal tumor spread was suspected in only 3 cases by CT, with histopathology demonstrating positive involvement in 2 other cases (Figs. 2, 3).

Cervical lympadenopathy was found by CT in 10 cases, with minimum node size being $1 \times 1.3 \times 1.2$ cm. The locations of these nodes were confirmed by histopathology, but lymph nodes were found to be metastatic in only 5 cases, while the others were found to be reactive.

Discussion

While total laryngectomy is still the most effective and radical surgical intervention for the therapy of laryngeal carcinoma, radiotherapy and conservative surgical techniques are equally effective for localized lesions in early stages. However, preoperative classification of a lesion to decide treatment modality requires exact determination of the location, size and extent of the tumor present.

Since only mucosal surfaces are visualized by laryngoscopy, tumor extension into submucosal, pre-epiglottic and paralaryngeal tissues can only be inferred by inspection from increased bulk or altered physiology. As such, tumor infiltration into "hidden" sites may remain undetected unless deep specimens are obtained by biopsy [11, 24]. As a consequence, other means are needed to diagnose tumor invasion into deep tissue planes and laryngeal cartilages or extension into the ventricles and subglottis. Large fungating supraglottic lesions can even make glottic and subglottic areas impossible to be seen [18].

In evaluating laryngeal masses CT findings provide additional information to conventional radiological investigations and are of great importance. CT also provides an imaging technique capable of a three-dimensional anatomical display of the larynx [1, 3, 4, 6, 21, 29]. While CT provides little information to demonstrate the anatomy of small, superficial lesions, it has a more important role in evaluating deep laryngeal and paralaryngeal soft tissues [12]. Multiple scans are required to obtain precise information about tumor infiltration into the deep tissue planes extending between mucosa and the laryngeal framework or into the framework per se. When used appropriately, CT can depict even slight differences between the similar densities of the laryngeal soft tissues, resulting in more precise information about tumor extension and replacing (especially in an axial plane) conventional radiological techniques [5, 8, 12, 21, 29, 33].

The complex anatomical configuration of the larynx presents certain problems in histopathological examina-

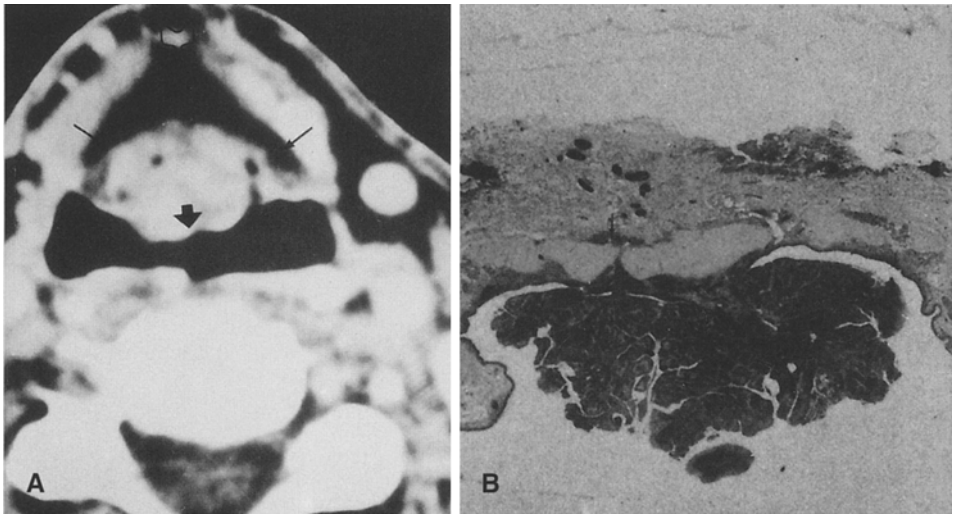

Fig. 4 Act scan at the level of the inferior margin of the hyoid bone. Bulky tumor mass originating from the mucosa of the epiglottis extends to the laryngeal vestibule *(large arrow)*. Tumor invasion into the epiglottic cartilage cannot be clearly defined. On this section PES (*open arrow*) and both PLS (*long arrows*) are seen as normal. **B** Histopathological specimen corresponding to the same level as the CT scan. Tumor can be seen adjacent to the inner surface of the epiglottic cartilage, with minor erosion (*arrowhead*) present in the cartilage. On the anterior surface of the epiglottic cartilage some inflammation (*small arrow*) is present, but there is no tumor invasion to the anterior surface of the epiglottis

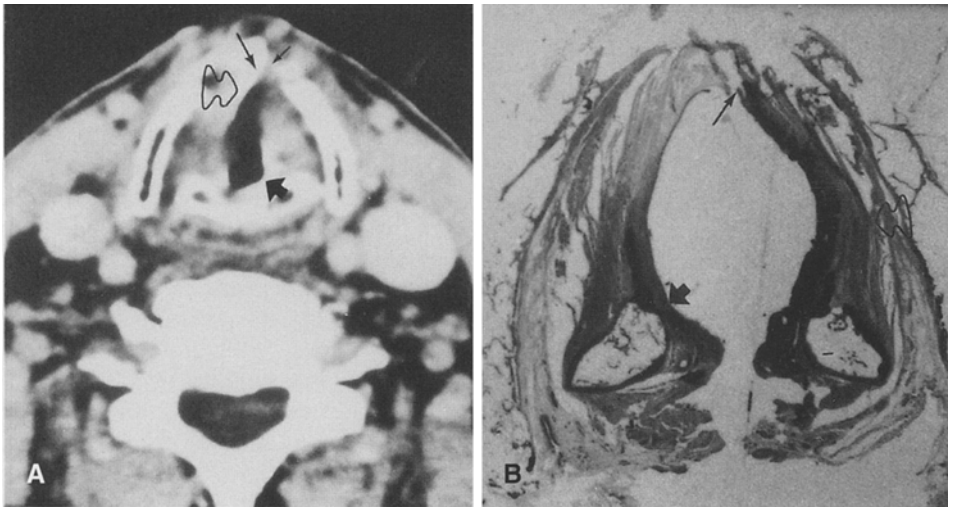

Fig. 5 Act scan at the level of the vocal cords. Some irregularity is visible on the mucosal surfaces of both vocal cords. The lesion on the right vocal cord extends to the anterior commissure (long arrow) and to the other vocal cord by crossing over the posterior commissure *(large arrow)*. Both PLS (*open arrow*) seem to be normal and there seems to be a small area of destruction (*small arrow*) on the left side of the thyroid cartilage. Both arytenoid cartilages are normal. **B** On the corresponding histopathological section, tumor does not invade the other cord by crossing the anterior commissure, but does involve the posterior commissure. However, tumor is only adjacent to both arytenoid cartilages and to the right lamina of the thyroid cartilage and has not invaded the cartilages

tion. To acquire precise information about tumor extension, multiple sections must be examined. However, routine serial sectioning of the whole larynx is much too difficult and far too time-consuming. The variations in density of the laryngeal tissues make the process more difficult, as do age-related ossifications in the laryngeal skeleton [1, 2, 30]. Nonetheless, comparison of CT scans with corresponding histopathological sections can determine objectively the clinical role of CT in defining the true extent of a tumor.

The paralaryngeal space

According to some authors, tumor infiltration into the PLS in the presence of thyroid cartilage destruction makes CT more valuable in diagnosis than conventional radiological investigations [10, 13]. The PLS is composed primarily of muscle and fatty tissue. Since tumor and muscle have the same densities on CT scans, it can be more difficult to discriminate one from the other. At the level of the vocal cords, the normal PLS is visualized as a fairly thin,

low-density zone lying between the cords and the medial surface of the thyroid cartilage. For this reason, unless tumor is large enough to produce distortion of normal anatomy, tumor invasion into the PLS may not be evident on CT [14]. Histopathological examination in our present cases demonstrated tumor invasion into the thyroid cartilage in 6 specimens and to the cricoid cartilage in 1 case in which we also determined tumor infiltration into the PLS. This PLS involvement was found with a high accuracy in an early stage in the majority of these cases, with only 1 case being misinterpreted on CT because of inflammatory changes. Indeed, it may not be possible to differentiate tumor from associated inflammatory and edematous changes on CT scans [30] because of slight differences between the densities of these tissues. This lack of differentiation may cause erroneous evaluation of tumor extent.

The pre-epiglottic space

Studies based on the comparison of CT tissue sections have stressed that CT can depict PES involvement with great accuracy rate [1, 3, 6, 9, 11, 14, 23, 31]. The PES is primarily composed of fatty tissues and has a special configuration and characteristic tissue density on CT scans [18, 27]. Deeply infiltrating tumor usually obliterates the normal low-density fatty content of this space [19, 29]. The obvious differences between the densities of tumor and fatty tissue make it easier to evaluate tumor invasion into the PES by CT. This was evident in our present study. As found in 2 of our cases, large tumors of the PES frequently undergo central necrosis, with changes possibly due to the relative avascularity of the fat that normally fills this compartment [15]. When large tumors of the PES penetrate the laryngeal framework (as occurred in 6 of our cases), modalities for therapy are negatively affected.

The laryngeal framework

Laryngeal cartilage invasion – whether by small or large lesions – means that tumor is about to or has spread outside the confines of the larynx. This situation necessitates more radical surgical interventions.

Thyroid cartilage

It is extremely difficult to use CT to detect cartilage invasion in cases that have limited lesions adjacent to the thyroid cartilage [5, 11, 14, 27]. According to some authors, while the determination of early cartilage invasion is hard to make by CT, gross cartilaginous destruction can be detected reliably by CT [14, 28]. However, the normally irregular and non-uniform patterns of calcification and ossification of the thyroid cartilage make it extremely difficult to evaluate early cartilage involvement, even using high-resolution CT [29, 30]. In contrast, uniform calcification and ossification of the thyroid cartilage (demonstrating a dense cortex and low-density medullary portion) allow cartilage boundaries to be easily seen on CT. Unfortunately, the latter situation may not be commonly found and anatomy is frequently asymmetrical [1, 17, 18]. Since less calcified cartilage can be poorly visualized it may simulate erosion or destruction [5, 29]. In contrast, tumor may also grossly invade the medullary space of the laryngeal cartilages and may not be detected if a sufficient number of bony trabeculae remain [30]. In Reid's experience [28], the general criteria for the CT determination of cartilage invasion rest upon breaks in the chondral margin of the cartilage adjacent to tumor and formation of a fenestrated border or, in advanced cases, an "explosion" of cartilages.

Histopathology of our present cases demonstrated tumor adjacent to the thyroid cartilage in 4 specimens with micro-invasion in 1 of the cases that was not detected by CT. In accordance with other authors' experiences, we concluded that it was extremely difficult to use CT to detect micro-invasion in cartilage or small lesions adjacent to cartilage. In contrast, larger tumor masses with gross cartilaginous destruction were easily detected by CT.

Cricoid cartilage

In evaluating tumor invasion into the cricoid cartilage, positive results were more readily determined by CT [5, 6, 14]. The cricoid cartilage is often well-calcified and its boundaries are more obviously seen on CT scans. As with the thyroid cartilage, the cricoid cartilage has a characteristic dense cortex and low-density medullary portion [18]. Our present series included 1 case of a large subglottic cancer with cricoid cartilage destruction. This was easily visualized by CT. Histopathology in 21 cases showed true correlations with CT scans and confirmed the absence of tumor invasion into the cricoid cartilage in these cases. Thus, these findings demonstrated that CT was extremely reliable for evaluating cricoid cartilage invasion.

Epiglottic cartilage

Unfortunately, the literature is sparse concerning CT examination of the epiglottic cartilage in cases with tumor invasion. This is probably because the epiglottic cartilage may not be visualized clearly by CT and involvement of the PES and PLS is more important than of the epiglottic cartilage itself. Furthermore, since the epiglottis is a thin fibroelastic cartilage, its subhyoid portion is very difficult to visualize on CT scans. In 4 out of 6 cases in which invasion of the epiglottic cartilage was determined on CT scans, tissue sections revealed tumor invasion of the PES, PLS and thyroid cartilage. For practical purposes, the demonstration of micro-invasion into the epiglottic cartilage by CT was almost impossible unless there was no distortion of the epiglottic contour.

Anterior laryngeal commissure

The anterior commissure can easily be evaluated clinically, so that imaging may be unnecessary for this area [20, 22]. While some authors believe that spread deep to the anterior commissure is reliably detected on CT scans, others have found that contrast laryngography is superior to CT for this area [29, 32].

Nonetheless, visualization of the anterior commissure on CT is characteristic and this area is well-evaluated by CT. Any tissue thickening of the intraluminal mucosa in this area should be considered to be abnormal although hemorrhage and edema can mimic neoplasia [21, 30]. To demonstrate actual tumor invasion into the anterior commissure, CT sections at 1.5–2 mm slice thickness are best used [15]. Certain mucosal tumors that appear to be small on direct laryngoscopy may have extended so deeply as to involve the thyroid cartilage. To confirm such situations we now prefer to use CT to evaluate the anterior commissure. In 3 of our cases in which anterior commissure involvement was detectable by CT, there was also thyroid cartilage invasion. Moreover, we have concluded that CT examination of the anterior commissure is extremely reliable in cases which have no overt deep tissue invasion.

Posterior laryngeal commissure

The posterior commissure is also reliably detected on CT [29]. Posterior carcinomas originating from the arytenoids and interarytenoid region have a tendency to extend subepithelially. The exact extent of these tumors is well delineated on CT, although scans performed during quiet respiration are essential for evaluating this region. During phonation (with cord adduction), the mucosa of the posterior commissure bunches up, simulating a pathological thickening [20]. When obvious tumor is detected in this location, subtle invasion of arytenoid and cricoid cartilages is present in about 20% of cases [29]. In all of our cases in which CT showed tumor "invasion" into the posterior commissure, histopathology revealed that tumor was actually located adjacent to the arytenoid cartilage. These findings demonstrate the limitations of CT in defining tumor invasion from one side to the other in the posterior commissure.

Subglottis

Subglottic tumor extension can easily be determined by direct laryngoscopy and frontal tomography [32]. However, CT is superior to conventional radiological investigations in ascertaining the upper and lower limits of tumor [2, 7, 11, 23]. These extensions are important, since an anterior subglottic extension of more than 1 cm and posterior extensions of more than 0.5 cm indicate the need for total laryngectomy [11, 28]. Deep subglottic extensions of glottic tumors cannot be evaluated accurately by laryngoscopy and this may cause false interpretations [11]. Furthermore, the relationship of tumor to the cricoid cartilage is of critical importance and can be visualized accurately on axial CT scans [20].

The extralaryngeal tissues

Laryngeal tumors tend to remain within the confines of the cartilaginous structures of the larynx [28]. A significant number of advanced or aggressive laryngeal tumors will spread to the extralaryngeal tissues and may not be easily palpated. Conventional radiological techniques do not reveal much information about extralaryngeal tumor spread [2], whereas CT can facilitate the depiction of this spread [22]. The infrahyoid strap muscles are easily seen on CT and tumor infiltration into these tissues can be visualized as increased tissue densities [2]. However, our findings have shown that CT is inefficient for determining micro-invasion into extralaryngeal tissues, but is useful for visualizing tumor infiltration with cartilage destruction.

Lymph nodes

Cervical lymph node metastases in laryngeal cancer may be occult or palpable [16]. Visualization of the common carotid artery with its bifurcation and the jugular vein facilitates detection of the location, size and number of lymph nodes. CT may be useful in identifying metastatic lympadenopathy in which the tumor has become adherent to the carotid artery [21]. CT can demonstrate non-palpable small lymph nodes [22, 25, 26], but cannot depict whether lymph nodes are metastatic or reactive unless there is an evident necrotic area [21, 28]. In our study, CT was best used to define cervical lymph nodes greater than 1 cm in diameter, but was inefficient for determining nodal quality.

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