G.J. Gerritsen – COMPUTED TOMOGRAPHY AND LARYNGEAL CANCER

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G.J. GERRITSEN

VRIJE UNIVERSITEIT TE AMSTERDAM

COMPUTED TOMOGRAPHY AND LARYNGEAL CANCER

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Promotor: Prof.dr. G.B. Snow
Copromotor: Prof.dr. J. Valk
Referent: Prof.dr. B.A. den Herder

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This study has been carried out at the departments of Otorhinolaryngology, Radiology and Pathology of the Free University Hospital, Amsterdam.

CONTENTS

INTRODUCTION

According to World Health Organization statistics, covering 35 countries an average of 1.2 persons out of every 100.000 inhabitants of these countries died of laryngeal cancer in the year 1961 (1). The incidence of laryngeal cancer seems to increase. In the Netherlands, in the period 1969-1978 a mortality rate of 2.3 was found in males (2). Today approximately 600 new larynx malignancies are diagnosed yearly in the Netherlands. The etiology of laryngeal cancer is unknown. Epidemiological studies have indicated a variety of predisposing factors such as smoking habits and irradiation of the neck. These studies have clearly demonstrated that cancer of the larynx rarely develops among men who do not smoke. The carcinogenic effect of radiation has been established definitely and the use of excessive amounts of alcohol plays a role in the etiology of, particularly the supraglottic cancer (3).

In the Netherlands most laryngeal cancers, about 2/3 of cases, are seen at the glottic region, whereas about one third is located at the supraglottic region. The subglottic localisation is extremely rare (4). Over 90% of all epithelial malignancies of the larynx are squamous cell carcinomas. The incidence of lymphogenic spread is related to the site of the primary tumor and its size. In supraglottic carcinomas lymphogenic metastases are seen in 30-55% of cases (4,5). Lymphogenic metastases of glottic carcinomas are rare.

The key to successful management of laryngeal cancer is early diagnosis and appropriate treatment applied when the extent of the lesion has been accurately determined. According to the UICC

Committee rules (6), laryngeal carcinomas can be classified by the TNM system. This system is based on the assessment of the extent of the primary tumor (T), the condition of the regional lymph nodes (N) and the absence or presence of distant metastases (M).

The "smaller" laryngeal carcinomas, T_1 and T_2, can be diagnosed reliably by clinical and conventional radiologic examination. High cure rates are obtained by radiation therapy as is well shown for instance by the five-year survival rates for T_1 and T_2 glottic carcinomas: respectively 90% and 70% (7). In supraglottic tumors conservation surgery can also provide excellent survival rates with good functional results.

However, the exact delineation of the extent of advanced tumors, T_3 and T_4, may present major problems. Cartilage invasion and extralaryngeal spread are often underestimated. In general, advanced tumors are treated by total laryngectomy. However, some investigators support a management policy to treat the advanced lesions also primarily by radiotherapy with salvage surgery in reserve (8,9). These authors estimate that the gain in survival rate by primary surgery does not justify the larger amount of laryngectomies with subsequent loss of vocal function.

From the foregoing it will be clear that there is a great need for a more differentiated management policy in advanced laryngeal cancers, which allows the choice of treatment to be made on the basis of accurate assessment of the extent of the lesion. Conventional clinical and radiologic examination give insufficient information on this regard. These methods usually fail in demonstrating cartilage invasion, infiltration into the laryngeal compartments and extralaryngeal spread.

CT scan, however, can provide valuable information in this respect, as the only method capable of visualising the extent of the laryngeal cancer in the horizontal or axial plane.

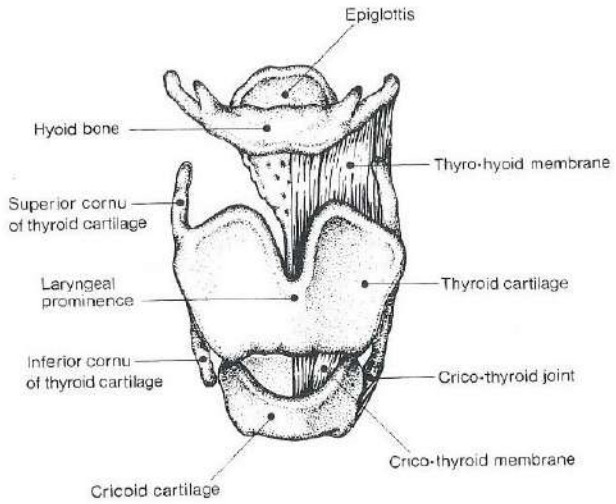
At the departments of otorhinolaryngology, radiology and pathology of the Free University Hospital of Amsterdam, a study has been carried out to evaluate the accuracy of CT scanning in determining the extent of laryngeal cancers, particularly of advanced lesions. The study is based on CT scan findings in 84 patients with laryngeal cancer.

Chapter I will cover the normal anatomy of the larynx. In Chapter II patterns of growth and spread of laryngeal cancer will be discussed. Chapter III deals with the routine clinical and conventional radiologic examinations. In Chapter IV the CT findings of the normal larynx will be illustrated and compared with scans of patients in whom cancer has altered the normal anatomy. In the second part of Chapter IV the findings in a group of 20 patients, in whom preoperative CT scan images have been carefully compared with corresponding histopathologic slices of their excised larynges, are demonstrated and discussed. In Chapter V the clinical impact of pathologic changes as seen on CT scan will be discussed in direct relation to the management policy of laryngeal cancer.

CHAPTER I

ANATOMY OF THE NORMAL LARYNX

The larynx is an organ of the respiratory system. The larynx is situated between the root of the tongue and the trachea. Anteriorly the larynx is covered by the infra-hyoid muscle group, fascia and skin. Posteriorly, the larynx is bordered by the constrictor pharyngeus muscle and the oesophagus. The upper part extends into the pharynx, the lower part is continuous with the trachea. The average length of the rima glottidis in the adult male is 23 mm and in the adult female 17 mm (10,11). The skeleton of the larynx consists of the hyoid bone, the thyroid cartilage, the cricoid cartilage, the arytenoids and the smaller cartilages (Fig. 1). Although the hyoid bone is sensu strictu not a part of the larynx, it is generally



Anterior view of cartilages and ligaments of the larynx **Fig.1**

included in it because of its relationship to the pre-epiglottic space (PES). The pre-epiglottic space and the paralaryngeal space (PLS) are of particular importance for the spread of laryngeal cancer (12,13,19).

The thyroid cartilage

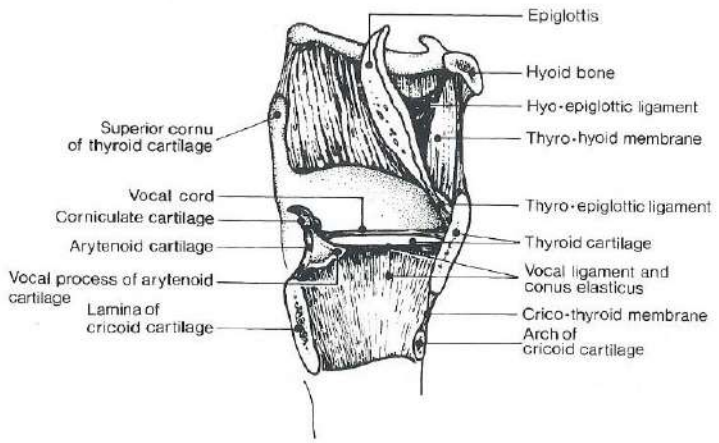
The thyroid cartilage consists of two main flattened pieces, laminae or alae, which fuse anteriorly in the midline (Fig. 1). Posteriorly it is composed of two posterior processes or horns, the superior and inferior thyroid cornua. The angle made by the two laminae is about 90 degrees in men and 120 degrees in women. In the male the fused anterior borders project as the laryngeal prominence or Adam's apple. The two laminae separate above the prominence to form the thyroid notch. The thyroid cartilage is attached to the hyoid bone by the thyro-hyoid membrane. The inferior horn of the thyroid cartilage points in a foreward and medial direction and articulates with the postero-lateral surface of the cricoid cartilage, the crico-thyroid joint. The inferior border of the thyroid is concave. The cartilage is covered by a layer of perichondrium except at the anterior commissure. Here, only a fibrous cord separates the mucosa from the cartilage. This cord has been described by Broyles as the anterior commissure tendon (14). In this small area the thyro-epiglottic ligament, the vocal ligament and the thyro-arytenoid muscle are attached.

The cricoid cartilage

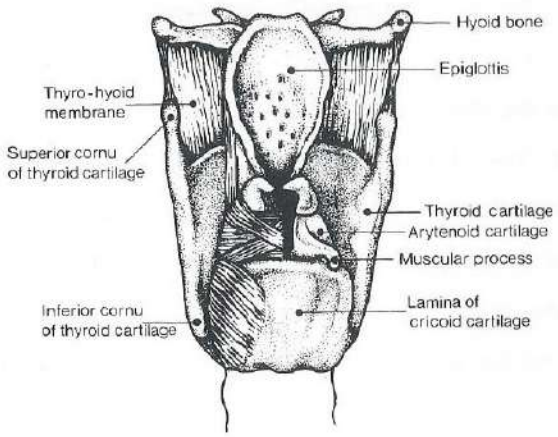
Inferior to the thyroid cartilage is the smaller cricoid cartilage (Fig. 1 and 2). The cartilage possesses a narrow anterior arch and a broad posterior lamina. The height of the anterior arch is approximately 6 mm. The inferior margin of the cricoid is horizontally and is connected to the upper ring of the trachea by the crico-tracheal ligament. The height of the posterior arch is approximately 25 mm.

The arytenoids

The two arytenoid cartilages are placed on the upper lateral borders of the cricoid cartilage (Fig. 2 and 3). They are pyramidal in shape. The base of the pyramid articulates with the cricoid cartilage, whereas the apex articulates with the corniculate cartilage. The anterior angle of the base of the pyramid forms the vocal process



Cartilages and ligaments of the larynx in sagittal section **Fig.2**



Posterior view of cartilages and ligaments of the larynx **Fig. 3**

to which the vocal ligament is attached. The medial surface is covered with mucous membrane. The posterior surface is covered by the inter-arytenoid muscle or transverse arytenoid muscle. At the lateral surface the muscular process of the arytenoid gives attachment to the thyro-arytenoid muscle and the posterior crico-arytenoid muscle. The lateral crico-arytenoid muscle is attached to the anterolateral surface of the muscular process.

The epiglottis

This is a lamella of elastic fibrocartilage. Its caudal end is connected by the thyro-epiglottic ligament to the thyroid laminae and the anterior commissure at a level below the thyroid notch. The superior margin is called the free edge. At the anterior surface of the epiglottis the mucous membrane forms in the midline the glosso-epiglottic fold with on each side the vallecula. The epiglottis

is connected to the hyoid bone by the hyo-epiglottic ligament (Fig. 2). The cartilage itself contains several defects in its structure known as the orifices cribiformes. On the posterior surface numerous glands are present in the mucous membrane.

Calcifications of the laryngeal cartilages are seen from the age of 20. Calcifications are frequently found in the lower portion of the thyroid cartilage. Later on they proceed superiorly. Calcification of the cricoid cartilage starts at the superior border. The cricoid cartilage is in general less calcified than the thyroid cartilage. The vocal process of the arytenoid does normally not calcify. Calcification of the arytenoid can be seen at older age. The impact of the calcification in the spread of laryngeal cancer and particularly in relation to the invasion of the cartilages will be discussed in the next chapter.

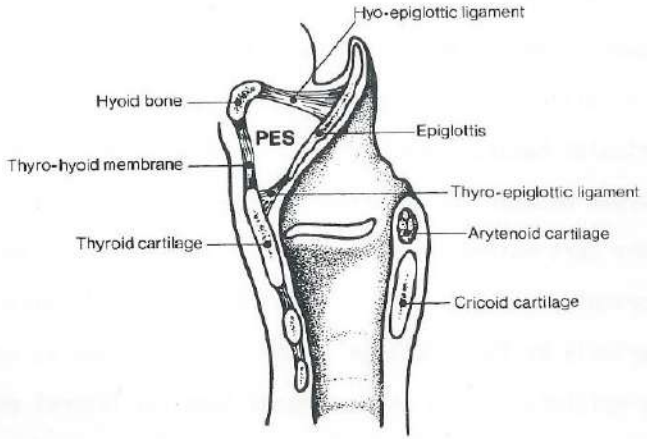
The cavity of the larynx

The cavity of the larynx extends from the pharynx at the laryngeal inlet to the lower border of the cricoid where the trachea begins. The cavity can be divided into a superior part, i.e. the vestibule above the ventricular bands, a middle part, i.e. the ventricle or sinus of the larynx between the ventricular bands and the vocal cords and a lower part extending from the vocal cords to the lower border of the cricoid cartilage. The inlet of the laryngeal cavity is bounded superiorly by the free edge of the epiglottis and on each side by the ary-epiglottic fold, which extends from the lateral edge of the epiglottis to the arytenoid cartilage. The vocal cords are

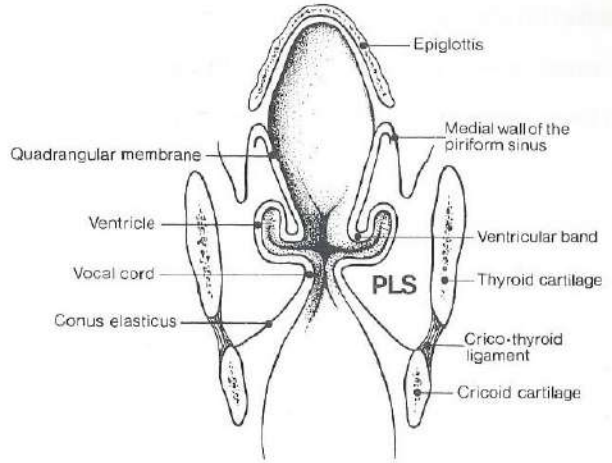
attached to the thyroid cartilage and to the vocal process of the arytenoid. They include the vocal ligament and the thyro-arytenoid muscle. The vocal ligament represents the thickened upper margin of the conus elasticus.

The laryngeal spaces

Important for the growth and spread of laryngeal cancers are the pre-epiglottic space and the paralaryngeal space. The pre-epiglottic space (PES) is bounded by the thyro-hyoid membrane, the hyo-epiglottic ligament, the epiglottis and the thyro-epiglottic ligament (Fig. 4). The thyro-hyoid membrane is attached below to the superior border of the thyroid cartilage and above to the upper margin of the posterior surface of the body of the hyoid. Its middle part forms the median thyro-hyoid membrane. The infra-hyoid muscles are found



Sagittal section of cavity of the larynx **Fig. 4**



Frontal section of cavity of the larynx **Fig. 5**

anterior to this structure. The thyro-hyoid membrane represents the anterior wall of the pre-epiglottic space. The roof of this space is formed by the hyo-epiglottic ligament. Its base is represented by the epiglottis with the thyro-epiglottic ligament (Fig. 4).

The paralaryngeal space (PLS) is the second potential space important in the spread of laryngeal tumor. This space is bounded laterally by the thyroid and cricoid cartilages with the crico-thyroid ligament and medially by the conus elasticus, the vocal cord, the ventricle, the ventricular band and the quadrangular membrane (Fig. 5). The paralaryngeal space is continuous with the pre-epiglottic space.

The conus elasticus

The conus elasticus is a well developed layer of elastic tissue that is attached to the upper border of the cricoid cartilage (Fig. 5).

It extends medially and upwards. Anteriorly in the midline, the two sides of the conus unite and are attached to the inner surface of the thyroid cartilage. Posteriorly the conus is attached to the arytenoid cartilage and its vocal process. The vocal ligaments are the thickened edges of the conus. The conus elasticus is an anatomic barrier against direct tumor spread.

The musculature

The muscles of the larynx can be divided into two groups: the intrinsic and extrinsic muscles. The intrinsic muscles modify the size of the vestibule, the ventricular bands and vocal folds. Important in the spread of tumor are the thyro-arytenoid muscle, the inter-arytenoid muscle, the crico-thyroid muscle and the posterior and lateral crico-arytenoid muscles. Only the crico-thyroid muscle is situated on the outer aspect of the larynx.

The thyro-arytenoid muscle is the most important muscle in relation to spread of laryngeal cancer. It arises from the thyroid cartilage and the crico-thyroid ligament. The fibers pass backwards, laterally and upwards to be inserted into the anterolateral surface of the arytenoid cartilage. The lower and deeper fibers form a bundle which is attached to the lateral surface of the vocal process. The thyro-arytenoid muscle adducts the vocal cords and rotates the arytenoid medially. Infiltration of tumor into the muscle results in impaired mobility or even fixation of the vocal cords.

The lymphatics

The lymphatics of the larynx are numerous. No lymphatics are found at the vocal cords. In this area the mucosa is very thin and tightly attached to the vocal ligament. The lymphatics can be divided into a superior and an inferior group. The area above the vocal cord is drained by the superior group, which drains on the internal jugular chain of nodes. The area below the vocal cord is drained by the inferior group of vessels, which drains on the recurrent nerve chain of nodes, the Delphian nodes and the pretracheal nodes (15).

The blood and nerve supply

The laryngeal branches of the superior and inferior thyroid arteries are important vessels for the blood supply of the larynx. The superior laryngeal artery supplies the muscles and membranes in the superior portion of the larynx. The inferior laryngeal artery supplies the lower part of the larynx. The arteries are accompanied by their veins. The nerve supply is derived from branches of the superior laryngeal nerve, the recurrent laryngeal nerve and from the autonomous nerve system (15).

CHAPTER II

THE PATTERNS OF GROWTH AND SPREAD OF LARYNGEAL CANCER

Introduction

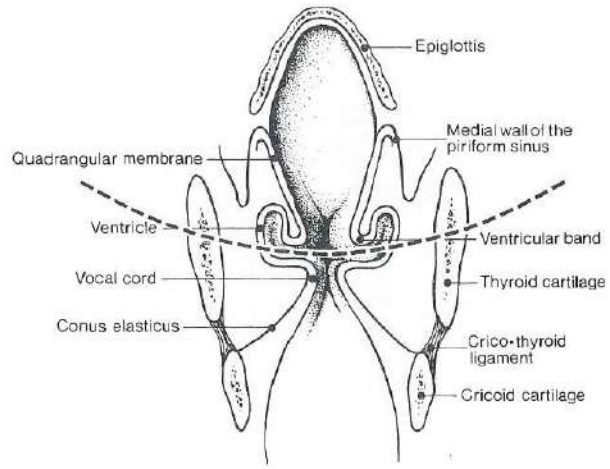
Clinical and conventional radiologic examination are often insufficient for exact delineation of the extent of the tumor, particularly in intramural forms without involvement of the mucosa (4). Histologic examination of large series of surgical specimens after laryngectomy yielded valuable information on the modes of invasion of laryngeal carcinoma (16,17,18,19,20). Growth and spread of laryngeal carcinoma are determined by the site of origin of the primary tumor. Local and regional spread is often mechanical in nature. Major factors in determining the direction and extent of the tumor growth are anatomical barriers produced by the laryngeal compartments, the anterior commissure, the cartilagenous framework and intercartilagenous membranes. Within these barriers there are strong and weak points, which may modify the diffusion of cancer.

The glottis exceeds all other areas as a site of predilection. About 2/3 of all laryngeal carcinomas are found at the glottic region. About 1/3 of the laryngeal carcinomas originate in the supraglottic region. Primary subglottic carcinomas are unusual, accounting for at most 4% of the total number of cases of laryngeal carcinoma. A topographical classification in which laryngeal carcinomas are divided into three anatomical divisions, supraglottic, glottic

and subglottic, is commonly used for a precise description of the extent of the primary tumor. Different modes of invasion will be discussed according to this topographical classification. Furthermore special attention will be paid to the infiltration in the anterior commissure, cartilage invasion, lymphatic spread and vascular and perineural invasion.

Cancer of the supraglottic region

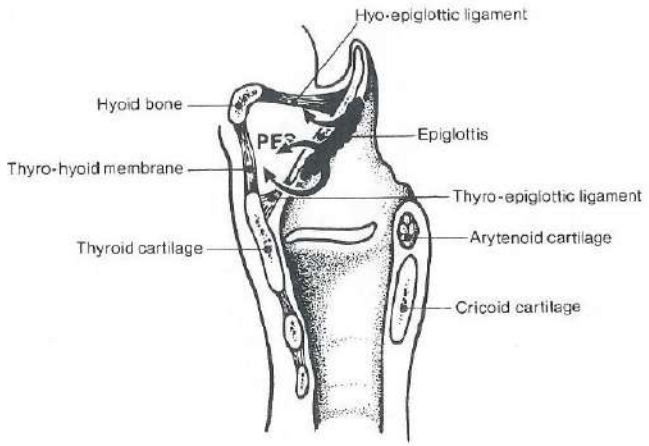
The supraglottic region is, according to the UICC-TNM classification rules (6), bounded inferiorly by the vocal cords and superiorly by the free margin of the epiglottis and by the ary-epiglottic folds. A horizontal line through the lateral angle of the ventricle is considered the boundary between the glottic and supraglottic regions (Fig. 6). Most cancers are found on the laryngeal surface of the



Frontal section of cavity of the larynx **Fig.6**

epiglottis and are localised in the subhyoid portion above the ventricle (22). The supraglottic cancers tend to be restricted to the supraglottic region. This appears to be related to the embryologic development of the larynx. The supraglottic portion develops from the buccopharyngeal anlage, while the glottic and subglottic portions develop from the tracheo-bronchial anlage (23). As reported by McGavran and his associates (24), supraglottic cancers tend to be less invasive than their counterparts in other parts of the larynx. It is generally accepted that supraglottic tumors have pushing margins and only rarely extend to the glottic region (22,24). However, spread to the glottic region may occur in carcinomas arising in the ventricle.

The spread of supraglottic cancer, originating at the laryngeal surface of the epiglottis, is superficial and bilateral. Invasion into the PES is not uncommon. The delineation of the PES has been mentioned before. Tumor spread into the PES can not be diagnosed reliable by clinical examination, neither is there a reliable



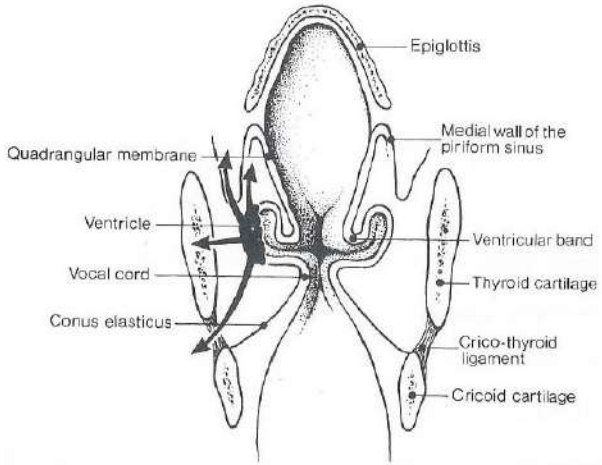
Sagittal section of cavity of the larynx Fig.7

conventional radiologic technique to demonstrate this growth pattern. Spread into the PES can take place in several ways (18,19,25,26). Direct passage of the tumor through the orifices of the epiglottic cartilage, destruction of the cartilage or spread through the thyro-epiglottic ligament are described (Fig. 7). The thyro-hyoid ligament and the hyo-epiglottic ligament are effective barriers against extralaryngeal growth.

The spread of carcinomas localised on the ventricular bands is limited. These lesions spread to the laryngeal surface of the epiglottis anteriorly or to the arytenoid posteriorly. Infiltration into the PES is rare, but involvement of the PLS is more frequently seen.

Supraglottic tumors do not directly invade the laryngeal framework itself unless the lower edge of the tumor extends to the level of the anterior commissure (18,20,22). However, cancer which invades the PLS can exhibit an agressive growth pattern by infiltrating the laryngeal cartilage and emerging from the confines of the larynx by direct extension between the thyroid and cricoid cartilage or by submucosal spread into the piriform sinus (Fig. 8). The term transglottic carcinoma is used for extensive deep tumor invasion passing the ventricle in a vertical direction with subglottic extension. All transglottic carcinomas are characterized by invasion into the PLS.

Spread of supraglottic tumors in horizontal direction into the PES or in vertical direction into the PLS is of utmost importance considering the indications for conservation surgical treatment or radiotherapy (27,28,29,30,31,32). Precise information

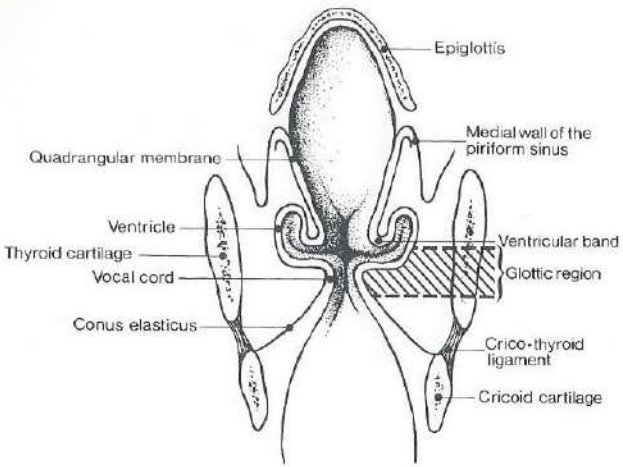


Frontal section of cavity of the larynx **Fig. 8**

on tumor spread must be obtained preoperatively. CT scan can provide us with information to select patients suitable for either conservation surgery or radiotherapy. The value of the CT findings in case of laryngeal cancer at the supraglottic region will be discussed in Chapter V.

Cancer of the glottic region

The glottic region is delineated anteriorly and posteriorly by the anterior and posterior commissure respectively. The lateral wall of the ventricle represents the superior border and the upper margin of the conus elasticus the inferior border (Fig. 9). Most of the glottic carcinomas arise on the free border of the vocal cord which is covered by squamous cell epithelium. There is a predelection for the anterior half of the vocal cords and for the anterior commissure.

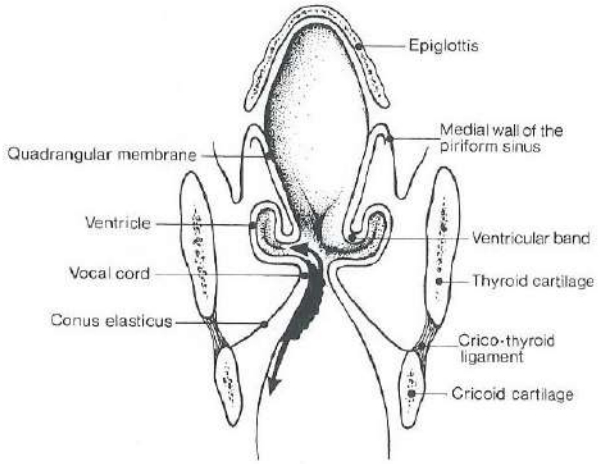


Frontal section of cavity of the larynx **Fig. 9**

The posterior commissure, the arytenoid and its vocal process are rarely primarily involved. However, posterior extension of a vocal cord lesion is possible medially or laterally to the arytenoid cartilages and sometimes results in destruction of the cartilages and the vocal process (18).

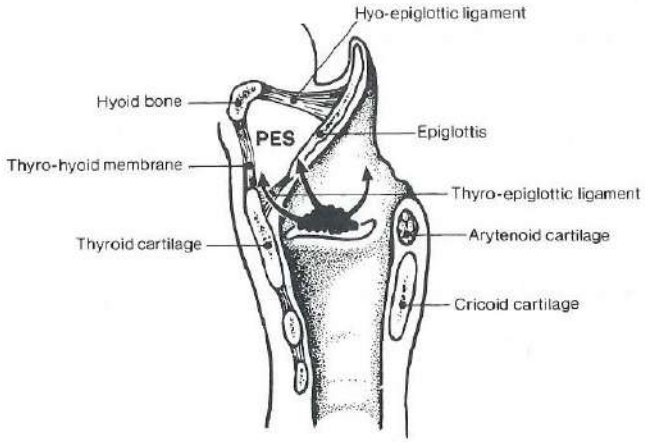
The spread of glottic tumors can be superficially or in depth, in vertical or in horizontal directions. When the spread is superficial the tumor follows the mucosal surface of the free border of the vocal cords. The inferior surface of the vocal cord is frequently involved and submucosal tumor spread into the subglottic region can be present (Fig. 10). The vertical extension of glottic tumors to the supraglottic or subglottic region occurs more frequently than the horizontal extension to the opposite side of the larynx (17,18,20).

Vertical extension of the glottic carcinoma to the supraglottic region is frequently related with destruction of the thyro-epiglottic



Frontal section of cavity of the larynx **Fig.10**

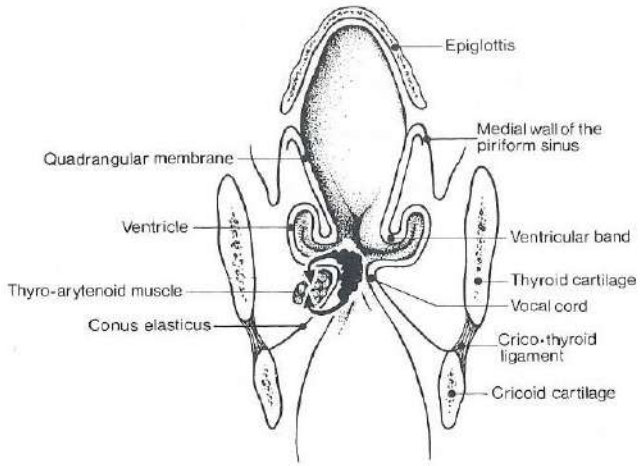
ligament and invasion into the pre-epiglottic space (Fig. 11). Inferior extension into the subglottic region is rarely found below the superior border of the anterior arch of the cricoid cartilage (19). Subglottic extension in the anterior commissure can result in



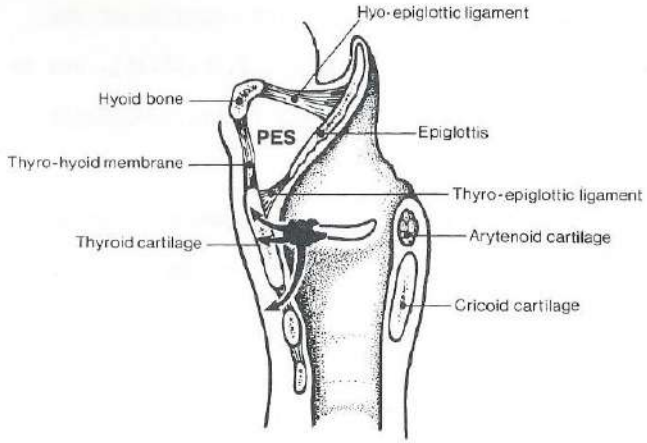
Sagittal section of cavity of the larynx **Fig.11**

destruction of the thyro-cricoid ligament and invasion of the prelaryngeal and pretracheal tissues (17,18,19,20,33,34). Due to a minor calcification the cricoid cartilage is not frequently infiltrated by tumor (19,32).

The glottic tumors involve, when they continue to enlarge, the paralaryngeal space. Extension into the paralaryngeal space is possible from any mucosa adjacent to the PLS. Hypopharyngeal tumors, arising from the medial or anterior wall of the piriform sinus, are also very likely to involve the PLS (19). Invasion of the PLS means a direct infiltration or destruction of the thyro-arytenoid muscle and the vocal muscle (Fig. 12). Infiltration of the thyroid cartilage combined with destruction of the crico-thyroid membrane permits extralaryngeal tumor spread. However, evident cartilage invasion and destruction with breakthrough of the thyroid cartilage and extra-laryngeal growth of the tumor is mostly seen close to the midline in



Frontal section of cavity of the larynx **Fig.12**



Sagittal section of cavity of the larynx **Fig. 13**

the anterior commissure region (37,38,39,40) (Fig. 13). The anterior commissure plays an important role in the spread of glottic carcinomas and therefore deserves special comment.

The anterior commissure of the larynx includes the area of the vocal cords insertion at the thyroid alae. The area is delineated by the upper surface of the vocal cords, superiorly and extends 5 mm subglottically. The horizontal boundaries of the area are formed by the thyroid cartilage at the insertion of the anterior commissure tendon and a free margin of 2 mm of the vocal cords in posterior direction.

Since 1943, when Broyles first described the anterior commissure tendon, it is known that laryngeal carcinoma often breaks through in the anterior midline (14). There are several reasons for this phenomenon related to the infavorable anatomical conditions of the anterior commissure region. If the tumor is located in the anterior

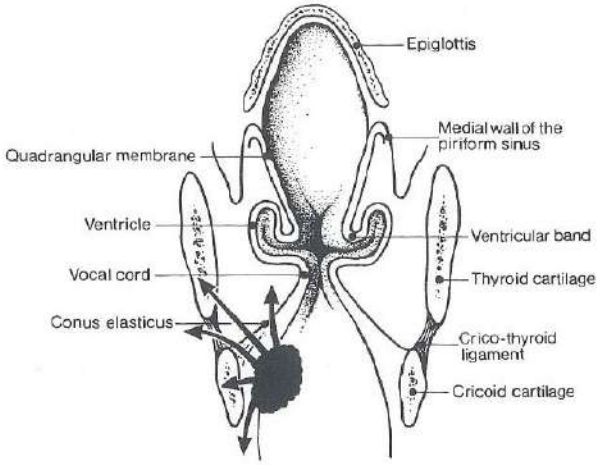
commissure it is close to the cartilagenous framework. In the anterior commissure there is no protective perichondrial lining inside the thyroid cartilage. In the midline, only a fibrous cord separates the mucosa from the cartilage.

According to Broyles findings and more recent serial sectioning studies by Olofsson (19,39), it is clear that the cord or tendon extends from the margin of the thyroid notch down to the level of insertion of the vocal ligament. The perichondrial lining is absent at the insertion of the tendon and tumor infiltration is very likely to occur. However, if tumor spread is confined to the tendon region, metastases to regional lymph nodes are rare, despite the presence of blood vessels and lymphatics. A second weak structure in the anterior commissure region is the crico-thyroid ligament and its insertion at the thyroid cartilage. Destruction of the ligament permits extra-laryngeal tumor spread and lymphatic spread.

Evaluation of involvement by tumor of the anterior commissure by conventional X-ray techniques has been proven to be a major problem of this diagnostic method.

Cancer of the subglottic region

The subglottic region is bounded superiorly by the upper margin of the conus elasticus and inferiorly by the lower margin of the cricoid cartilage (41). The conus elasticus extends from the upper border of the cricoid to the vocal cord where it represents the vocal ligament. Subglottic tumors tend to spread through the conus



Frontal section of cavity of the larynx **Fig.14**

elasticus into the paralaryngeal space (Fig. 14). They usually do not involve the mucosa of the free margin of the vocal cords. Early spread of the disease into the deeper part of the vocal cord will therefore not be detected. Subglottic lesions frequently infiltrate the thyroid and cricoid cartilages. The incidence of invasion, particularly into the thyroid cartilages is 50% or higher (19,20,39). In contrast to supraglottic tumors, subglottic tumors frequently have a submucosal spread with ill-defined outlines. In posterior direction unsuspected submucosal extension can be found below the level of the cricoid with destruction of the tracheal wall and invasion of the cervical oesophagus. Undetected extension and the tendency to an early extralaryngeal growth, without interfering with cord mobility, give the explanation for inaccurate classification of these tumors.

Cartilage invasion

Thyroid cartilage invasion occurs most frequently in the lower and middle thirds of the anterior part of the thyroid lamina (20). Glottic tumors tend to invade the thyroid cartilage in the anterior commissure. As discussed before, the perichondrium is deficient where the anterior commissure tendon attaches the cartilage. Invasion of the cartilages is a well known feature of the transglottic carcinoma.

The mechanism of invasion is explained by Kirchner (18,20) and is based on the modes of ossification of the laryngeal cartilages. In most cases, in which cancer invades the cartilage, the invasion is confined to the ossified portions of the cartilage. The ossified areas are better vascularised than the non-ossified portions of the cartilage. The frequency of invasion is related to bone metaplasia, often seen in elderly patients. Infiltration into metaplastic areas evokes a local increase in the number of osteoclasts. These cells destroy the bony patches by resorption in front of the invading tumor. The mechanism is the same as that seen when squamous cell carcinoma invades true bone (42,43,44,45). Infiltration of non-ossified cartilage by tumor is uncommon due to the absence of microvascularisation in the intercellular chondroid substance, the existance of a resistant perichondrial layer and the absence of osteoclasts. Some authors suggest that squamous cell carcinomas provoke osteoclasts activity and that local factors are released for the resorption of ossified cartilage (42.44).

While connective tissue membranes are generally considered as barriers against spread of laryngeal carcinomas, studies of histopathologic sections have suggested that the same barriers may serve as routes for invasion of the cartilages (46). This mechanism of invasion will be described.

Histologic sections of cartilages in the early stages of invasion show cancer cells growing between collagen bundles of the ligaments and membranes where these are attached to the cartilage (46,47). The attachments of the crico-thyroid membrane, the vocal ligament and the anterior commissure tendon are the most common places. The collagen bundles pass through the entire thickness of the perichondrium and enter the cartilage directly, creating an entrance for tumor invasion. The same mechanism is found at the attachment of the crico-arytenoid joint. The perichondrium itself is a strong barrier to tumor invasion, which is illustrated by the fact that despite marked lifting or displacement, the perichondrium in most cases is still intact. Large masses of tumor may press against the perichondrium with no evidence of invasion. Detection of cartilage invasion is of great clinical importance. Complications of radiation therapy such as perichondritis, necrosis and subsequent severe edema, are likely to occur when cartilage invasion is present. Demonstration of such an invasion therefore may contribute to better selection of treatment methods. Until the advent of the CT scan, cartilage invasion could be diagnosed only very rarely. CT can accurately demonstrate cartilage invasion when this is associated with extralaryngeal tumor spread. However, CT can not detect early cartilage invasion (48).

Lymphatics

Squamous cell carcinomas of the mucous membrane of the head and neck in general and those of the larynx in particular have a preference for the lymphatic route of metastasis. The incidence of lymph node metastases is dependent on the site of origin and the extent of the primary tumor. The degree of histologic differentiation of the squamous cell carcinoma has also been mentioned as a factor of importance. McGavran has shown that lymphatic metastases are more common when the primary neoplasm is greater than 2 cm. However, the presence of cartilage invasion or invasion into the laryngeal compartments and destruction of membranes and ligaments is not always associated with a higher metastatic rate (24).

Knowledge of the pathways of lymphatic spread is essential for interpretation of the soft tissue findings on CT scan. Studies of Pressman et al (17) demonstrated that the lymph drainage system of the larynx is divided into two compartments according to the embryologic development, which has been discussed before. Some vessels of the superior part pierce the thyro-hyoid membrane and reach via the thyro-hyoid plexus the cervical nodes near the bifurcation of the common carotid artery. Others pass through the floor of the piriform sinus, along with the superior laryngeal artery and join the nodes of the chain along the internal jugular vein (49,50). Therefore, visualisation of the common carotid artery with its bifurcation and visualisation of the internal jugular vein on CT scan can help to interpret position, size and number of the adjacent nodes. The vessels of the

inferior part form three pedicles. The anterior pedicle pierces the crico-thyroid membrane, drains on the crico-thyroid plexus and passes downwards with the inferior laryngeal artery to the prelaryngeal or Delphian nodes, the pretracheal nodes and the recurrent nerve chain of nodes. Some of these reach the supra-clavicular nodes where they join the nodes of the chain of the jugular vein. Two posterolateral pedicles pierce the crico-tracheal membrane and drain on the paratracheal nodes and then finally into the superior mediastinum (15,49,50).

On CT scan the configuration of the trachea and the related soft tissue structures can be visualised (51). Pathologic and normal deep cervical nodes can be scanned. CT scan demonstrates capacity to show non-palpable enlarged nodes (51,52,53).

Vascular and perineural invasion

Vascular invasion was less frequently found in serial sections by Olofsson et al than expected (19). If the tumor is confined to the glottic region no vascular invasion is seen. Vascular invasion can be found in the subglottic region especially in glottic tumors with a subglottic extension. The invaded vessels are found immediately beneath the conus elasticus. Vascular invasion of lymph node metastases in the main vessels of the neck can be demonstrated in selected cases. Therefore, preoperative visualisation of lymph node metastases in relation to these vessels is important.

Perineural invasion of laryngeal carcinoma is sometimes found

when the lesion infiltrates deep into the PLS and into the connective tissues deep to the thyro-arytenoid muscle near the lower end of the thyroid ala. In this particular region the branches of the recurrent laryngeal nerve are present.

Different growth patterns and modes of invasion of laryngeal carcinomas require careful preoperative evaluation of the extent of the tumor. The next chapter, therefore, deals with the conventional diagnostic evaluation of laryngeal cancer.

CHAPTER III

CLINICAL AND CONVENTIONAL RADIOLOGIC EXAMINATION OF THE LARYNX

CLINICAL EXAMINATION

Clinical examination of the larynx includes indirect laryngoscopy, direct laryngoscopy and external examination. Each of these methods adds a different type of information.

Indirect laryngoscopy

The image seen in the mirror is a reflected one. As the mirror is positioned the examiner will observe the base of tongue, the anterior surface of the epiglottis, the valleculae, the hypopharyngeal wall and the upper part of the piriform sinus. By tilting the mirror the examiner notes the free margin of the epiglottis, its laryngeal surface, the ary-epiglottic folds and the posterior commissure. Under phonation the aspect and mobility of the ventricular bands and vocal cords are examined. The subglottic region can be observed and several tracheal rings, but these areas can not be evaluated completely by mirror examination alone.

Indirect laryngoscopy offers an excellent preliminary overall survey of the larynx and does not interfere with normal mobility of the laryngeal structures. However, the limitation of indirect

laryngoscopy is the inaccessibility of certain recesses of the larynx, where serious disease may lie undetected. The undersurface of the ventricular bands, the lateral extent of the ventricles, the undersurface of the vocal cords, the postcricoid region and the apex and medial wall of the piriform sinus are inaccessible areas. In addition to the problem of inaccessibility of several regions, there are variations in patient's response to the procedure. In some patients anatomic factors interfere with mirror examination. A most common difficulty involves an overhanging epiglottis. Mirror examination is unsuitable for anxious patients. In children indirect laryngoscopy is unsatisfactory.

Direct laryngoscopy.

Direct laryngoscopy is usually performed under general anaesthesia. The ideal anaesthetic technique provides an unobstructed view in a distorsion free direct vision alignment. To fullfil these conditions, the venturi jet ventilation system with positive air pressure has been developed as a modern technique in anaesthesia. The system permits the use of a small intra-laryngeal tube (54,55). A number of instruments are available for direct laryngoscopy. The operating microscope is an indispensable completion to the examination of small abnormalities.

The inaccessible areas of indirect laryngoscopy become more accessible by direct laryngoscopy. The ventricular bands can be displaced by the tip of the laryngoscope, the ventricles can

be inspected and the subglottic space can be observed. The piriform sinus can easily be exposed. Instruments can be used to palpate the intralaryngeal structures. This type of examination reveals a good deal of information about localisation, volume and extent of the intralaryngeal lesion.

Fiber-optic laryngoscopy is a new revolutionary method for intralaryngeal examination. The fiber-optic scope transmits images and light over curved pathes by utilising long thin fibres of optical glass. The scope can easily be introduced. Local or topical anaesthesia of the mucous membranes of the nose, oropharynx and larynx is usually sufficient. In children additional sedative medication is sometimes required. With the small flexible scope a good view of the intralaryngeal structures can be obtained. The undersurface of the ventricular bands, the lateral extent of the ventricles and the undersurface of the vocal cords, however, still remain more or less inaccessible. The visualisation of these recesses depends on the flexibility of the scope. The mobility of the vocal cords can easily be examined. Today the value of fiber-optic laryngoscopy is widely acknowledged (56).

External examination.

Much can be learned by external examination of the larynx and adjacent structures. Broadening of the larynx on palpation is a sign of advanced local tumor growth. Tenderness of the larynx

may denote laryngeal chondritis. Fullness of the crico-thyroid membrane or thyro-hyoid membrane suggests extralaryngeal tumor spread. Digital palpation is of importance to detect submucosal tumor extension into the base of the tongue.

Careful examination of the neck must be performed to detect any metastatic lymph node. It is well known that the presence of metastatic lymph nodes plays an important role in the prognosis. Size and number of involved nodes, mobility versus fixation, homolateral versus contralateral or bilateral involvement are important factors of prognostic significance.

Information obtained, in case of a laryngeal carcinoma, by clinical examination makes it possible to delineate the intralaryngeal extent of the disease and helps us to describe size and volume of the primary tumor. None of these procedures will show us the exact spread and invasion into the laryngeal compartments, into the cartilages or spread outside the laryngeal framework.

CONVENTIONAL RADIOLOGIC EXAMINATION

Introduction

Radiologic examination of the larynx is an indispensable adjunct to mirror and direct laryngoscopic examination. It has definitely been shown that radiologic techniques enhance the preoperative diagnosis of laryngeal lesions (57,58,59,60). The diagnostic accuracy of direct and indirect laryngoscopy leads to a correct

preoperative diagnosis in about 2/3 of cases. The addition of X-ray studies increases this result.

The main goal of radiologic examination is determination of site, size, extent and character of the laryngeal lesion and determination of functional alteration of the involved strutures. This includes, particularly, visualisation of areas which are inaccessible to mirror examination and determination of changes in specific areas of direct importance for growth and spread of laryngeal tumors. These specific areas are the ary-epiglottic folds with both arytenoids, the laryngeal compartments, the anterior commissure region, the laryngeal cartilages and the subglottic region. Radiologic studies should be performed before direct examination or biopsy of the lesion. A correct interpretation demands examination of all films. Only a persistent abnormality can be regarded as significant. Comparison of structures of both sides is essential in the interpretation of frontal projections.

Techniques

There are several radiologic techniques for the evaluation of laryngeal carcinoma. The following techniques are currently most commonly used: the soft tissue films of the neck, frontal tomography of the larynx and contrast laryngography.

Soft tissue films.

Soft tissue films are routine. The lateral view reveals much about

the status of the hyoid bone, the thyroid and the cricoid cartilages, the soft tissues of the larynx with adjacent areas and the air column. When taken with good technique a lateral film can show the outline of the base of tongue, the ary-epiglottic folds, the arytenoids, the ventricles and the subglottic space. Prevertebral soft tissues are demonstrated on these films. However, the topographic details afforded by the soft tissue films are inssuficient.

Frontal tomography.

Frontal tomography of the larynx was first described by Leborgne in 1936 (61). Tomography is a special radiologic technique to show in detail images of structures lying in a predetermined tissue plane while blurring detail of images of structures of other planes. The principle of tomography implies a coordinated movement of a focal spot and film, or an object and film, or a focal spot and object during the exposure. The first method is most frequently used. The focal spot and the film move in opposite directions and speed which bear a constant relationship to one another. The film, during this movement, remains parallel to its original position.

Frontal tomography gives good visualisation of the piriform sinus, the ventricular bands, the laryngeal ventricles, the vocal cords and the subglottic angle, based on the fact that these structures lie with their long axis perpendicular to the direction of the tomographic trajectory. Frontal tomography allows the laryngeal structures to be viewed free from their overlying structures (Fig. 15). The films are

taken during phonation and during inspiration with or without valsalva manoeuvres.

In literature, several fundamental rules for the interpretation of the tomographic views are mentioned (62,63,64). The vestibule of the larynx should be consistently symmetric in the normal situation. The ventricular bands, the ventricles and the vocal cords are also always symmetric in position under normal conditions. Obliteration of the laryngeal ventricle or subglottic extension of a vocal cord lesion can readily be visualised. During phonation and valsalva manoeuvres the inferior margin of the vocal cord and the subglottic angle are well visualised. The subglottic angle is sharp, symmetric and is almost a right angle in the normal situation. The lateral walls of the piriform sinus are slightly asymmetric but the medial walls should again be symmetric in absence of disease.

The valleculae and the ary-epiglottic folds are not clearly

fig.15

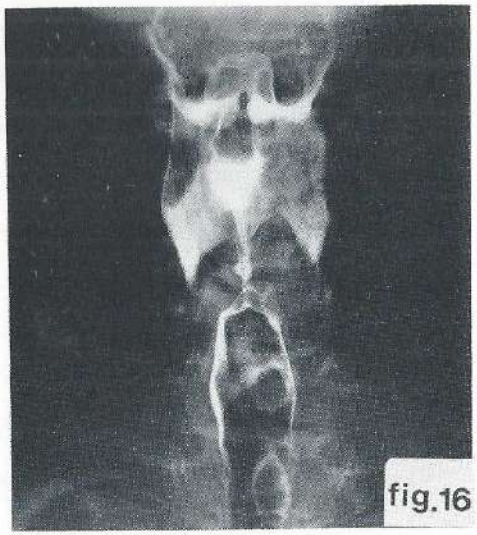


fig.16

delineated by frontal tomography. Destruction of the thyroid cartilage can only be suspected on these films. Lesions close to the anterior or posterior wall are not well seen in antero-posterior projections. Tomography adds little to the evaluation of supraglottic lesions. Tomography provides a good demonstration of size and contour of the vocal cords but a small tumor may not be visualised by this method. On the contrary, contrast laryngography can demonstrate almost all small intralaryngeal lesions (65,66,67,68).

Contrast laryngography.

This technique demonstrates the laryngeal and hypopharyngeal topography and gives information about the functional dynamics of the laryngeal and pharyngeal structures. The method has been described in detail by Landman (68). Patients with an allergy to iodine compounds and topical anaesthetics should be excluded from the procedure.

Routine X-ray films are taken with modified and regular valsalva manoeuvres (Fig. 16). Any degree of stridor due to laryngeal obstruction is an absolute contraindication.

It is generally assumed that tomography is a reliable technique in ascertaining the true extent of the glottic and subglottic disease, while laryngography is most important in the evaluation of supraglottic lesions.

Examination of specific areas

The ary-epiglottic folds and arytenoids.

A lesion of the free margin of the ary-epiglottic fold is mostly a circumscript soft tissue mass protruding into the vestibule or piriform sinus. However, before the tumor can be recognised on the X-ray film it is usually an extensive lesion. Extension into the piriform sinus can be detected by tomography or laryngography which is shown as an asymmetry in comparison to the other sinus. If the tumor involves the arytenoid the laryngogram demonstrates enlargement of the arytenoid. Destruction can not be visualised, neither by tomography nor by laryngography.

The pre-epiglottic space.

Pre-epiglottic space involvement can not be evaluated adequately on the lateral soft tissue film. Extensive spread and destruction of the epiglottis may sometimes be evident on these films. Tomography adds little to the evaluation of pre-epiglottic spread. Laryngography can precisely delineate the intralaryngeal extent of a lesion of the laryngeal surface of the epiglottis. It is, however, not useful for the demonstration of tumor invasion into the pre-epiglottic space.

The paralaryngeal space.

Invasion into the paralaryngeal space can be demonstrated by conventional tomography. Exact extension can not be delineated. Findings such as obliteration of the ventricle, changes in contour

of the medial wall of the piriform sinus and blunting of the mucosal lining of the subglottic angle may contribute to the diagnosis of paralaryngeal tumor invasion.

The anterior commissure.

Anterior commissure involvement is difficult to examine on lateral soft tissue films of the neck and is almost never shown by tomography. Infiltration into the anterior commissure can only be evaluated on the lateral inspiration manoeuvre of the laryngogram, if this method can be carried out succesfully. Failure of this area to be filled with contrast medium may suggest tumor involvement of the anterior commissure.

The laryngeal cartilages.

Invasion of the thyroid cartilage can be suspected on tomographic films. Tumor infiltration, however, is never precisely visualised. Laryngography and soft tissue films are also of minor value in this respect.

The subglottic region.

Subglottic invasion or submucous subglottic spread is fairly well demonstrated by frontal tomography. The use of phonation scans and valsalva manoeuvres adds information about subglottic tumor involvement. The subglottic angle then may become obtuse on the tomographic film. This finding can, however, also be present in cases of vocal cord fixation. Small subglottic tumor extension in the anterior or posterior wall is not visualised by frontal tomography.

We may conclude that clinical examination and conventional radiologic examination reveal much information about the extent of laryngeal carcinoma, particularly the intralaryngeal growth pattern. Tomography and laryngography supplement the information obtained by mirror examination and are of special interest for areas which are inaccessible for clinical examination. However, several specific areas important for growth and spread of the infiltrative tumors can not be visualised by the conventional techniques. None of the conventional methods gives the clinician an adequate view of tumor spread in the horizontal or axial plane. None of these techniques gives a detailed delineation of tumor invasion or destruction of the laryngeal framework. Therefore deep invasion and tumor spread outside the larynx is not accessible preoperatively by these conventional radiologic techniques.

CHAPTER IV

COMPUTED TOMOGRAPHIC EXAMINATION OF THE LARYNX

Introduction

In this chapter the principles of CT scanning will be shortly reviewed. Thereafter CT scan images of both the normal larynx and of pathologic changes of the larynx will be demonstrated.

Analysing the CT images of the pathologic larynx it appeared that certain tumor characteristics could be established. To further evaluate the reliability and significance of these a study was done in which the histopathologic changes of larynx specimens with laryngeal cancer were compared with the preoperative findings of CT scanning. This study will be reported in this chapter.

General aspects of CT scanning

Computed tomography is a synonym for computer aided image reconstruction of X-ray absorption. The principle of computed tomography was first described by Hounsfield (69). The system can be divided into a patienthandling part, an X-ray tube with a detector system and an image-reconstruction system. A collimated X-ray beam is sent through the part of the body under examination. The X-ray source turns around the patient. Detectors measure the absorbed

amount of X-ray photons. These measurements are digitised, processed and used for reconstruction of the image. Due to the fact that the CT image is composed from views at different angles no superposition of structures is found on the tomograms similar to the conventional tomograms. The main advantage of the CT scan system over conventional X-ray techniques is the resolution of small differences in density, such as exists between body fluids, tissue and fat.

In the first two generations of CT scan systems the improved resolution of small differences in density could be considered as a revolutionary improvement of X-ray imaging. The development of the third and fourth generation of CT scanners has shown that also high spatial resolution can be obtained in images made by the digital CT scan principle. The third and fourth generation systems have data aquisition times between 4 and 10 seconds for the high resolution mode.

Compared with the scanning times of 40 - 80 seconds of the first and second generation scanners this is of great importance, because most patients can reasonably be expected to hold their breath during this period. Despite the gain in spatial resolution CT scan systems still have difficulties in handling larger differences in density (bone-air). This remains a source of artefacts.

Scanning of the airways in the neck has therefore some disadvantages. There is a great difference in tissue density of the structures of the neck. This may result in artefacts reinforced by swallowing and breathing. Images of the larynx in patients with laryngeal cancer will often show some degrading due to these artefacts.

The display of the image of the monitor is a reflection of the

relative absorption of X-rays in each picture element (pixel) of the matrix. The digital values are stored in the memory of the computer. The image, as seen on the monitor, can be manipulated in different ways by setting the "level" and "window width". Direct measurements of the Hounsfield units per pixel or per region are possible as are measurements of the size of a lesion.

The level setting defines the center of the number of Hounsfield units displayed, whereas the window setting represents the actual number of displayed Hounsfield units. For example, with a level of 100 Hounsfield units the center of the numbers displayed is 100. With a window setting of 200, 100 Hounsfield units at each side of this level are displayed. This means that the grey scale is distributed over the Hounsfield unit values 0-200. Let us assume that the grey scale represents 20 shades of grey. In the given example that would mean that one shade of grey is available for 10 Hounsfield units. Before differences can be seen between two tissues the minimal difference therefore should be greater than 10 Hounsfield units. All pixels with a Hounsfield unit value below 0 will be black on the display. All pixels with a Hounsfield unit number over 200 will be white and contain no specific information. However, measurements remain possible in these areas. A change of the level and window setting can display visual differences between structures that are now solid black or white.

In the laryngeal region we have to visualise cartilage (+250 HU), air (-1000 HU), fat (-70 HU) and soft tissues (+40 HU). These variations make it necessary to display the images at a relatively high level setting with a relatively large window width. Tissues

representing the same or nearly the same number of HU's can not be separated visually on the scan film. The distinction between normal and pathologic tissue representing the same number of HU's is therefore impossible. Intravenous contrast is one of the means by which one can try to still differentiate between tissues of the same number of HU's due to differences in contrast medium uptake. In the pathology involving the larynx we have found intravenous contrast injections not helpful in differentiating normal from pathologic tissue. Intravenous contrast is helpful in localizing the vessels of the neck and to identify pathologic lymph nodes. Most information on the larynx is therefore of a morphologic nature such as distortion of structures, changes in tissue planes, asymmetries and abnormal configurations of tissue-air transitions.

CT of the normal and pathologic larynx

In a period of three years (1980-1983) we made approximately 84 CT scans of patients with laryngeal carcinoma. All CT scans were done on a third generation rotation scanner, Philips tomoscan 300 and 310. Sections with a slice thickness of 6.0 mm, 4.5 mm or 3.0 mm were made with a scanning time of 4.8 sec. The scan images were studied and the results were compared with those of the clinical and conventional radiologic examination. During this study it seemed worthwhile to obtain a histopathologic verification of the CT scan findings. Therefore we analysed 20 cases of laryngeal carcinomas. The CT findings of these cases were carefully studied and compared with the corresponding histopathologic slices of the excised larynges. The results will be

discussed and seven cases will be presented.

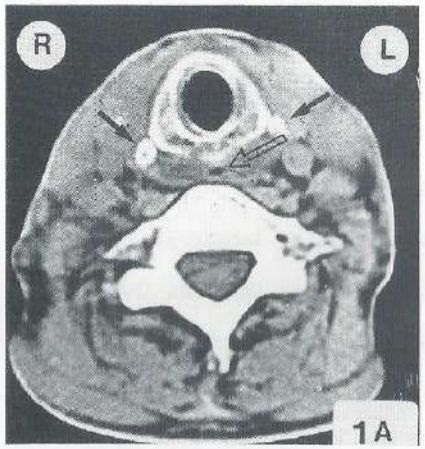
Reading the scan one should be aware that the patient's right side is on the reader's left side. To get familiar with the anatomy of the CT images of the larynx, at the various horizontal levels, it is helpful to use the laryngeal cartilages as landmarks. We, therefore, will start with illustrations of scan sections through these cartilages. The three laryngeal regions, the subglottic, the glottic and the supraglottic region can be related to these cartilages directly. The anatomic presentation of the cartilages also makes the configuration of the laryngeal compartments in the horizontal plane more understandable. We will, therefore, demonstrate the images of these compartments in direct association with the illustrations of sections through the cartilages. The normal scan views of both the cartilages and compartments will be compared with pathologic changes of these structures at each scan level.

Finally we will discuss the role of CT in the demonstration of soft tissue structures of the neck and the visualisation of normal and abnormal lymph nodes.

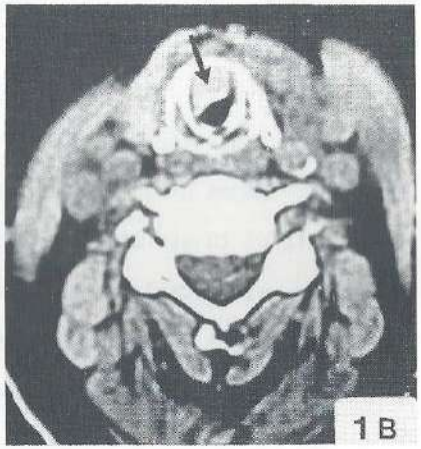
The cartilages

The cricoid cartilage

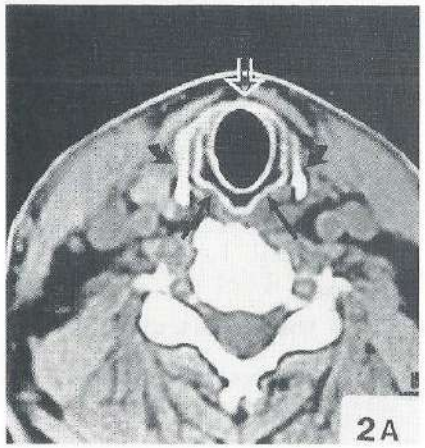
The appearance of the cricoid cartilage marks the section level of the subglottic larynx. At the low subglottic level the cricoid cartilage is a complete ring (Fig. 1a). The anterior arch is thin. At this level, at both sides, the cornu inferior of the thyroid cartilage is as a rule clearly visible lateral to the cricoid cartilage (Fig. 1a,



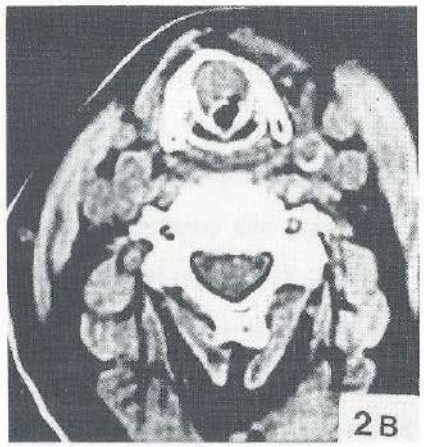
1A



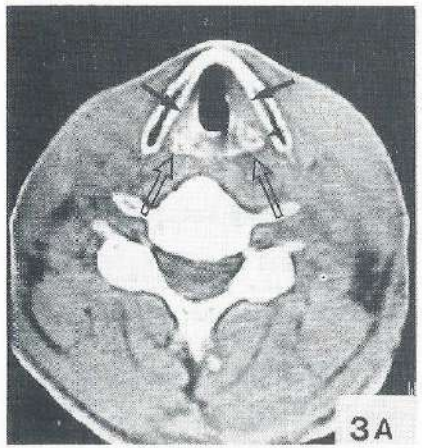
1B



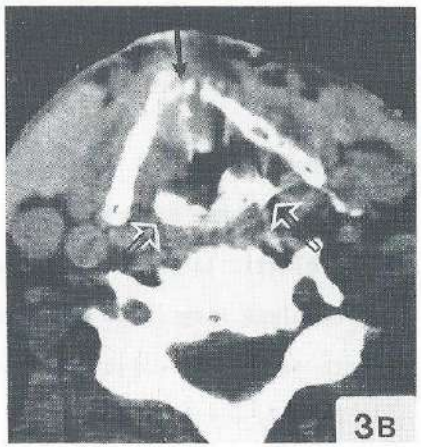
2A



2B



3A



3B

closed arrows). They identify the lowest part of the subglottic region.

On a more cephalad level, the cricoid cartilage has the appearance of an "U". It forms at this level an incomplete ring surrounding the posterior portion of the airway (Fig. 2a). The broader posterior portion of the cricoid is well recognised on the scan. The cricoid cartilage has defined margins (Fig. 2a, closed arrows). In adults the cartilage is partly calcified. The center, however, nearly always represents a low density zone and is in most cases not calcified. The intraluminal mucosal lining is firmly attached to the cricoid ring. Any thickening of this tissue structure is abnormal. At the high subglottic level the crico-thyroid membrane can sometimes be visualised anteriorly (Fig. 2a, open arrow).

Fig. 1b illustrates how pathology can alter the normal anatomy considerably. The scan demonstrates an intraluminal subglottic density as a result of a glottic carcinoma with large subglottic extension. The subglottic lumen is extremely narrow (Fig. 1b, closed arrow). The cricoid ring can be recognised clearly and does not seem to be destructed by tumor growth.

At the high subglottic level (Fig. 2b) the tumor is still clearly visible. The configuration of the cricoid ring is comparable with Fig. 2a. No destruction of the crico-thyroid membrane can be visualised. At this level no extralaryngeal tumor growth is demonstrated on the CT scan. The scan confirmed our clinical examination. Direct laryngoscopy revealed a large laryngeal carcinoma at the glottic level situated in the anterior commissure and on the anterior half of both vocal cords with clear subglottic

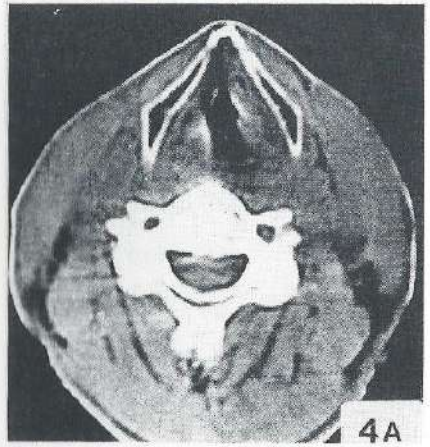
extension. The subglottic intralaryngeal lumen was markedly narrowed by the process.

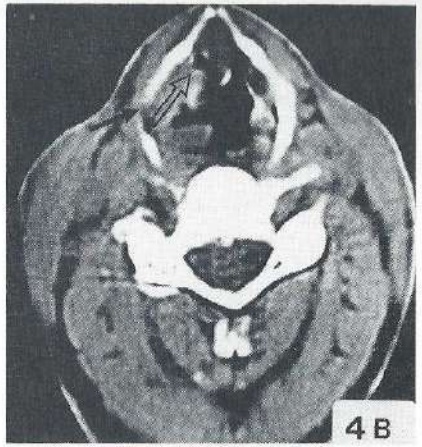
The thyroid cartilage

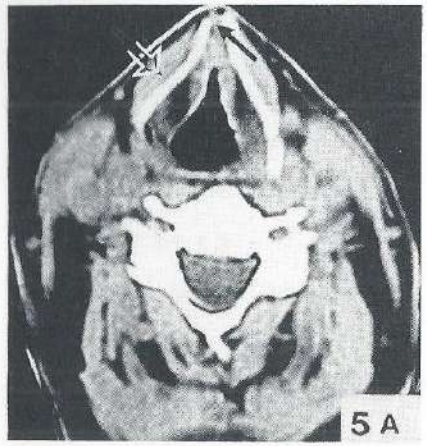
At the high subglottic level the contours of both laminae of the thyroid cartilage are found lateral to the cricoid cartilage (Fig. 2a, curved arrows). At a more cephalad level the thyroid laminae are increasingly prominent and a more typical V-shape of the laminae anterior to the intralaryngeal soft tissues is a CT landmark for the level of the vocal cords (Fig. 3a). A second important marker indicative for the vocal cord level is the relationship of the arytenoids to the cricoid cartilage. Fig. 3a reveals both radiodense configurations represented by the arytenoids (open arrows). At this level the cricoid is no longer recognised as a posterior ring.

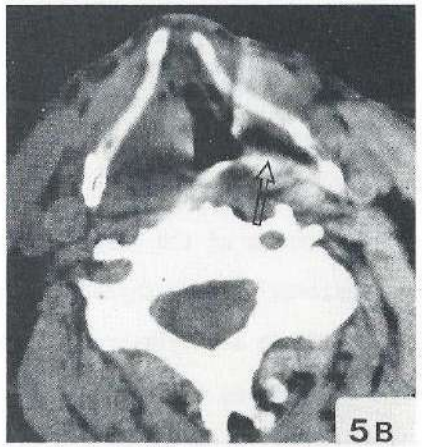
In the anterior commissure the mucosa should be adherent to the thyroid cartilage. Any tissue thickening in the anterior commissure region at this level can be regarded as abnormal. If the patient is examined in a correct position the laminae of the thyroid cartilage should be almost symmetric. Calcification of the thyroid cartilage is frequently seen and has to be interpreted as a normal finding. The degree and the extent of calcification of the thyroid cartilage vary considerably.

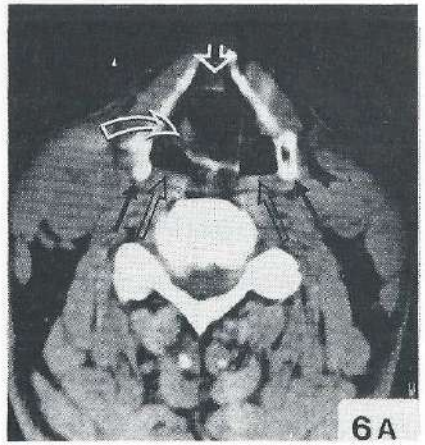
At a higher level the thyroid cartilage changes again in configuration (Fig. 4a). At this level the laryngeal ventricles should be found. They are, however, not recognised as distinct structures on the scan. Frontal tomography is still the method of choice for visualisation of these structures.

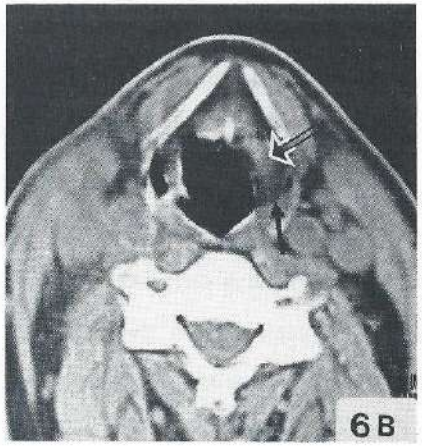












On the scan the thyroid notch can be recognised about one cm above the glottic region as a small characteristic gap, illustrated by Fig. 5a (closed anterior arrow). This structure is a typical landmark for the configurations of the upper aspect of the level of the ventricular bands. The paramedian part of the thyroid laminae can be very thin at this level. In this case the thyroid cartilage seems to be completely calcified.

On a more cephalad level the thyroid notch widens. The thyro-hyoid membrane can not be recognised on the scan at this level. Postero-laterally both superior cornu of the thyroid cartilage are found (Fig. 6a, closed arrows). The piriform sinus can be recognised as air-filled radiolucent structures (Fig. 6a, open arrows). At the supraglottic level we also find the infrahyoid strapmuscles anteriorly on the outside of the laryngeal framework. They create a soft tissue band external to the thyroid laminae (Fig. 5a, open arrow).

Fig. 3b-5b are illustrative for pathologic changes as demonstrated at corresponding scan sections. Due to a glottic carcinoma, a complete abnormal configuration of the anatomy at the glottic level is demonstrated. The contour of the posterior part of the cricoid ring, with two corresponding radiodense structures at both sides representing the arytenoids (Fig. 3b, open arrows), is indicative of the level of the vocal cords. A tumorous mass disturbs the anatomy completely and destroys the thyroid cartilage in the anterior commissure (closed arrow). Although defined delineation of extralaryngeal tumor growth is not visualised on the scan, extralaryngeal tumor growth in the anterior commissure region is very likely to have occurred. This statement is based on our experience in the interpretation of

tumor extension in case of a complete destruction of the cartilage in the anterior commissure. This will be demonstrated by the illustrations of a comparative study described later in this chapter.

Our CT findings did correspond well with the clinical examination. In this particular case a large ulcerative process could be seen on indirect and direct laryngoscopy. The lesion was found on the right side at the glottic and high subglottic level. The anterior commissure was replaced by a tumorous mass. In fact, no cartilage destruction could be seen and no extralaryngeal growth seemed to be present on palpation. Submucous infiltration of the right ventricle was found by direct laryngoscopy.

Fig. 4b shows a tumor process at the level of the laryngeal ventricles on the right side (note the asymmetry between left and right). The intralaryngeal lining appears to be irregular due to an ulcerative tumor mass. The scan section suggests the right ventricle and the anterior commissure region have been replaced by tumor. The right ala of the thyroid cartilage seems to be invaded (Fig. 4b, closed arrow). The sacculus of the laryngeal ventricle can be recognised as an air-filled lucency (Fig. 4b, open arrow). Direct laryngoscopy and frontal tomography demonstrate a transglottic process on the right side. The tumor extended into the anterior commissure region.

At the next scan level (Fig. 5b), that of the ventricular band, asymmetry between the right and left side is again clearly present. The piriform sinus appears to be partly obliterated, probably as a consequence of the submucous tumor extension. On CT scan an air-filled lucency is visible on the left side (Fig. 5b, open arrow), representing

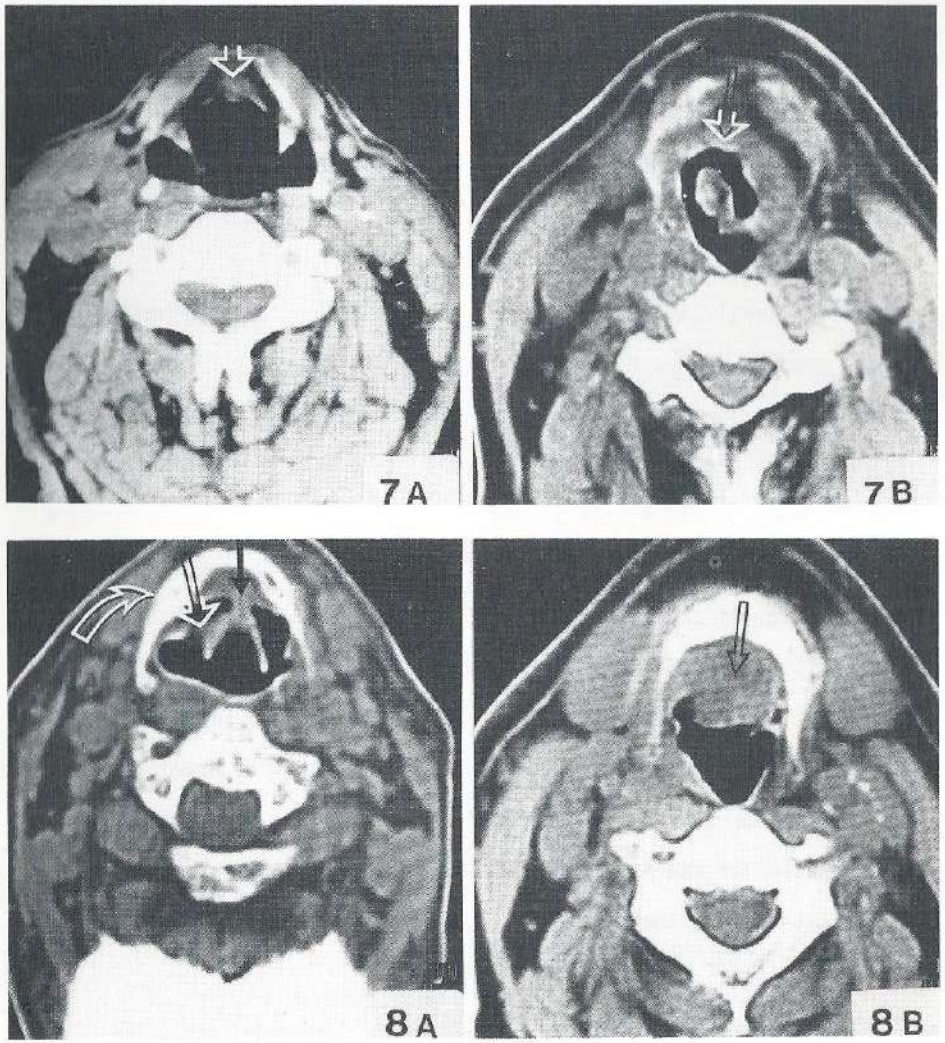
the most caudal part of the piriform sinus.

For adequate interpretation of asymmetric configurations of the piriform sinus, one should be aware of the normal anatomic variations due to variations in distension of the sinus. In this particular case, however, where a transglottic process was diagnosed by direct laryngoscopy and frontal tomography, the obliteration of the contour of the piriform sinus is very likely a consequence of submucous tumor growth on the right side.

The epiglottis

The base of the epiglottis, which is attached by the thyro-epiglottic ligament to the thyroid cartilage, can be recognised at the level of the thyroid notch (Fig. 6a, open anterior arrow). The cartilage of the epiglottis is rarely calcified. The posterior surface of the epiglottis is recognised as the anterior border of the laryngeal vestibule (Fig. 7a).

At a higher level (Fig. 8a), the free portion of the epiglottis can also be recognised on CT scan. Adjacent structures such as the valleculae divided by the glosso-epiglottic fold (Fig. 8a, closed arrow) lie anterior to the free margin of the epiglottis. The pharyngo-epiglottic fold can be visualised as a soft tissue band, extending from the lateral margin of the epiglottis to the lateral pharyngeal wall (Fig. 8a, open arrow). Asymmetry in presentation of the pharyngo-epiglottic fold has to be considered as normal, unless adjacent pathology is likely to be present. Under such circumstances differentiation between tumor infiltration and reactive edema can be a major problem.



The hyoid bone

The image of the hyoid bone can be composed of one or two scan sections. The hyoid bone can be partly calcified. The bone is visible as a clear radiodense structure on the scan (Fig. 8a, open curved

arrow). It is an important landmark for basic orientation and indicates the upper aspect of the pre-epiglottic space.

The laryngeal compartments

The paralaryngeal space (PLS)

At the level of the vocal cords the PLS forms, together with the vocal cord, a narrow tissue band (Fig. 3a). This soft tissue band is separable of the thyroid lamina by a thin low density zone (Fig. 3a, closed black arrow). Pathology can alter the aspect of this thin zone. The thyro-arytenoid muscle is not delineated as a distinct structure in the PLS. At a more cephalad level, the soft tissue band of the PLS widens (Fig. 4a and 5a). Infiltration of tumor and tissue thickening can easily be recognised as pathologic (Fig. 4b and 5b).

At the highest level of the PLS the space extends into the ary-epiglottic fold (Fig. 6a, open curved arrow). At this level the piriform sinus represents the postero-lateral boundary of the PLS. Obliteration of the sinus can be a result of submucous tumor infiltration into the PLS.

The pre-epiglottic space (PES)

The PES is recognised as an area of low density. The density is compared with that of fatty tissue (Fig. 7a, open arrow) and is slightly less than that of the PLS. The roof of the PES is found at the level of the hyoid bone and is represented by the hyo-epiglottic ligament. This structure can not be visualised. The base of the space is formed by the insertion of the thyro-epiglottic ligament. This ligament also,

is not recognised as a distinct structure on the scan. Tumor infiltration into the PES is usually associated with a major alteration of the contour of the epiglottis. Tumor growth into the PES increases the tissue density of the PES clearly.

Fig. 6b, 7b and 8b are indicative of pathologic changes at corresponding levels. These three scan sections represent a single case report. The clinical examination of this patient revealed a supraglottic laryngeal carcinoma. Direct laryngoscopic findings indicated a tumor mass at the laryngeal side of the epiglottis with destruction of the epiglottis. Submucous infiltration into both valleculae was found. Infiltration of the left ary-epiglottic fold also seemed to be present. The ventricular bands and both vocal cords were tumor free.

Fig. 6b demonstrates a tissue thickening of the upper aspect of the PLS on the left side, represented by an increased tissue density of the ary-epiglottic fold (Fig. 6b, open arrow). Obliteration of the left piriform sinus is visualised as a result of submucous tumor infiltration of the medial wall of the sinus (Fig. 6b, closed arrow). Increased tissue density of the PES is also clearly visible on the scan due to infiltration. The intralaryngeal lining of the epiglottis is irregular as a consequence of the ulcerations of the tumor.

At a higher supraglottic level (Fig. 7b) the contours of the epiglóttis are completely disturbed by tumor tissue. In our study we sometimes found central necrosis of the PES in case of tumor infiltration. In this case also, the process shows complete destruction of the epiglottis and necrosis of the PES (Fig. 7b, open arrow). At the level of the hyoid bone (Fig. 8b) clear extension into

the PES is present again and the normal anatomy is completely disturbed (Fig. 8b, open arrow). The valleculae are infiltrated. The glosso-epiglottic fold can not be visualised as a distinct structure and the hyoid bone seems to be intact.

The presentation of the last three scan sections illustrates how CT scan demonstrates intralaryngeal tumor extension and infiltration into the laryngeal compartments. In most cases the laryngeal framework is still intact. The framework seems to act as an anatomic barrier in determining the extent of the tumor growth. However, this is not to be considered as a general rule. Later in this chapter, when we compare the CT images with the corresponding histologic sections, more extensive destruction of the laryngeal framework will be illustrated.

The soft tissue structures of the neck

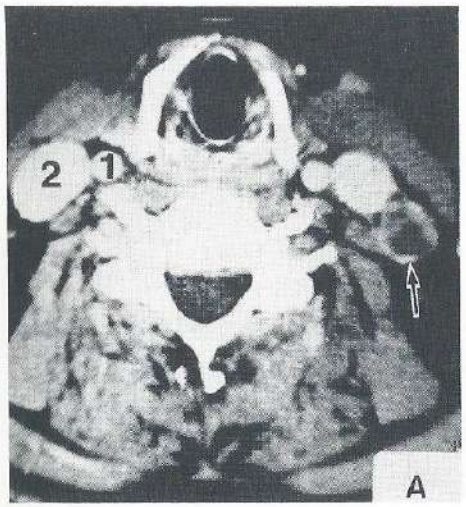
Although we have focused in our study primarily on the localisation and local spread of primary laryngeal tumors, it seems worthwhile to consider CT images of the extralaryngeal soft tissue structures of the neck as well. The analysis of images of these structures is based on identification of constant symmetry of paired structures such as deep fat planes, compartments, muscle groups and vessels. The fascias of the neck are not recognised as distinct structures. However, the compartments they create are useful CT landmarks in case of tumor spread of the primary lesion outside the larynx and in case of nodal metastases. The thyroid gland can be identified at the level of the upper trachea while the oesophagus can be recognised as a round mass

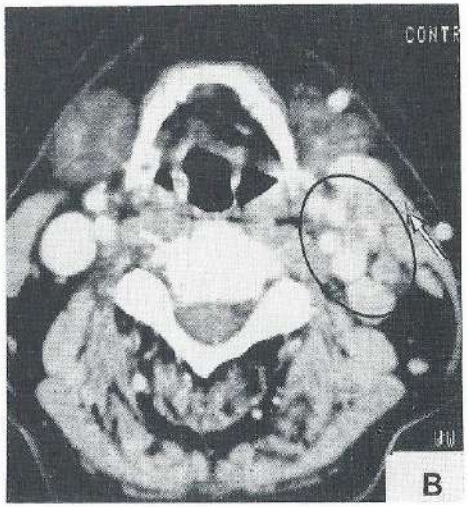
of increased tissue density posterior to the trachea. Occasionally, a small amount of air is seen in its lumen (Fig. 1a, open arrow). Horizontal images of muscle groups can be interpreted, taking into account the local anatomy of the neck at the various levels.

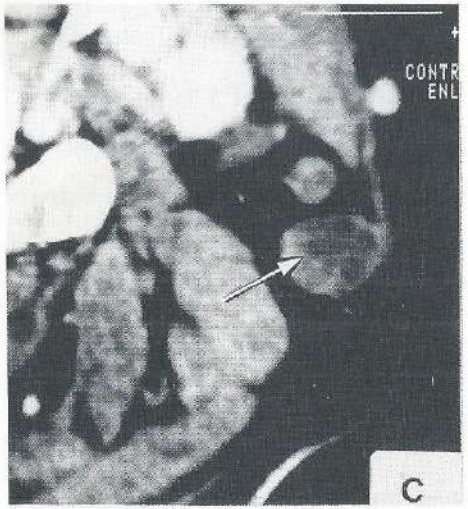
Lymph nodes

Lymph nodes can be scanned from the base of the skull to the thoracic inlet. CT scan only indicates possible number, aspect and localisation of regional nodes. These are all anatomic parameters. As yet there are no definite parameters to differentiate between reactive or metastatic nodes on CT scan. Opacification of blood vessels by angiographic techniques improves the identification of lymph nodes (Fig. A). The common carotid artery and jugular vein can easily be visualised (Fig. A 1 and 2). The jugular vein is always lateral to the carotid artery. In this particular case at the supra-glottic level, a group of nodes is visualised on the left side around the carotid artery under the sternomastoid muscle (Fig. B, circle and closed arrow, the arrow represents the muscle).

At the glottic level an irregular mass with a central lucency can be identified in close relation to the jugular vein (Fig. A, closed arrow). At the subglottic level, a second irregular mass is present and should be interpreted as abnormal (Fig. C, closed arrow, the section view is enlarged 2 times). As long as a central lucency and an irregular delineation are uncommon findings, these nodes can be interpreted as abnormal. These illustrations also suggest that CT scan can help identifying the ipsi- and contralateral nodes lying under-







neath the sternomastoid muscle in the deep tissue planes of the neck, which are not readily palpable by external examination.

A comparative CT-histopathologic study

Introduction

It is clear that structural abnormalities on the scan always have some explanation. However, alterations are not always a result of tumor growth. In case of pathologic changes as a result of tumor growth, our aim is to determine which findings on the scan have the potential to influence the therapeutic approach and which findings are of prognostic significance. To settle these issues an adequate comparison of CT images with a corresponding histologic examination is desirable to delineate the extent of the lesion and to verify the abnormalities as seen on the scan with proven precision. Such a study was conducted in 1982. In this study 20 cases of squamous cell carcinoma of the larynx were investigated. In the following discussion the methods of histologic examination of the larynx will be described. Thereafter, seven illustrative cases will be presented and evaluated. CT examination will be compared with the clinical and histopathologic examination.

Methods

Histologic examination of the larynx presents problems related to the complex anatomical configuration. To get precise information about the extent and spread of the tumor, multiple sections are required. The methods of whole organ sectioning have been described previously by other investigators (18,19,21,33,70,73). After decalcification

the larynx was cut serially in order to determine the precise nature of the tumor extension. The introduction of the CT scan requires a series of horizontal sections of the larynx specimen to be taken at intervals corresponding to the chosen distance between the CT images.

Michaels and Gregor (72) have described a slicing machine which quickly and easily produces material for an accurate gross study of the larynx. At the histopathologic laboratory we used an equivalent machine, slicing the specimen in horizontal sections with intervals of 6.0, 4.5 or 3.0 mm in correspondence with the CT scan.

After the surgical extirpation, the larynx specimen was photographed and fixed by immersion in a 4% buffered formaldehyde solution (pH 7.2). The specimen was left intact with the hyoid bone attached in order to gain a better understanding of the relation of the tumor to the hyoid bone. Decalcification was achieved by immersion in Kristensen's solution for approximately two weeks. After this procedure the specimen was prepared for slicing.

A horizontal cut was made between the thyroid and cricoid cartilage corresponding to the scan section at this particular level. Slices were made in a superior and inferior direction.
By means of this procedure the extent and typical growth pattern of the tumor in horizontal direction could be analysed macroscopically and microscopically. All slices were photographed.

The macroscopic examination included examination of the site of origin of the lesion, the extent of the lesion and all additional abnormalities seen on the scan. The microscopic examination included study of the complete histologic section with special attention being paid both to suspect abnormalities detected by CT scan but not by

macroscopic examination, and to macroscopic suspect abnormalities seen by serial sectioning but missed on the scan. The following case reports illustrate the results of these investigations.

Case reports

Seven case reports will be presented according to the TNM classification of the UICC, 1978 (6). The presentation includes three glottic carcinomas clinically staged as T_1N_0, T_2N_0 and T_3N_1, two supraglottic lesions staged as T_1N_0 and T_2N_0, a subglottic lesion T_2N_1 and finally a piriform sinus lesion.

Each case report includes a description of findings derived from the clinical examination, the CT scan and the histopathologic investigation. The clinical findings will be illustrated by an "artist-drawing", representing the extent of the lesion as seen by indirect laryngoscopy. The CT findings will be illustrated by the scan images themselves. The histologic findings will be presented by the photographic illustrations of the corresponding horizontal macroscopic and microscopic sections. Each report also includes a "comment", referring to the value of the CT in the evaluation of the extent of the lesion in that particular case. The reader should be aware of the fact that the right side of each scan image is on the reader's left side, whereas the right side of the histologic section is on the reader's right.

CASE I – A T_1N_0 glottic lesion

At our institution small glottic carcinomas are treated by radiotherapy. Therefore, we could only examine recurrences after radiotherapy, in the evaluation of small glottic carcinomas. The first case for presentation illustrates such a recurrent lesion of the right vocal cord. The patient, a man aged 56, had previously received radiotherapy for a small lesion, classified as a $T_{1a}N_0$ glottic carcinoma of the right vocal cord.

Clinical examination

Indirect and direct laryngoscopy revealed a tumor recurrence of the middle one-third of the right vocal cord. No evident ulceration was present. However, decreased mobility of the cord seemed to be present. No abnormalities were seen on the left side. The subglottic

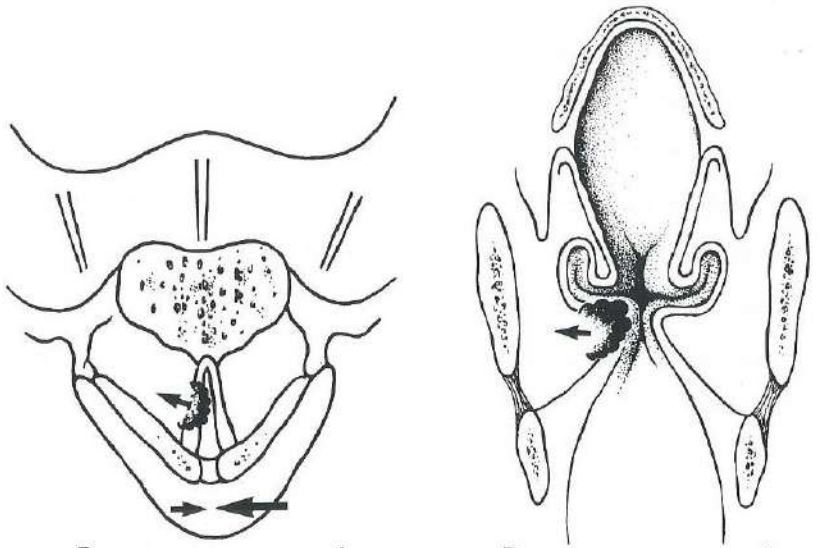
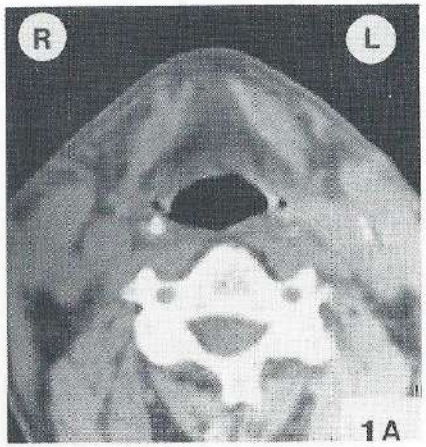


Fig. I

and supraglottic regions appeared completely normal. The clinical findings are illustrated by Fig. I . Deep biopsies were positive for squamous cell carcinoma, indicating the need for a total laryngectomy.

CT and histologic examination

At the high supraglottic level the tumor could not be seen either by means of CT scan, macroscopic or microscopic histopathologic sections (compare Fig. 1a, 1b and 1c). Rather, the PES appears completely normal on all three sections. On the next slice the CT scan again reveals no abnormalities (Fig. 2a). The thyroid cartilage appears to be intact, although a varying degree of calcification can be recognised. Both PLS are symmetric and of a comparable density. The macroscopic examination is normal. Microscopically, however, a small tumor field can be recognised in the anterior commissure (Fig. 2c, closed arrow). This small abnormality was missed both on the scan and the macroscopic section. Microscopic examination indicates intact cartilages and clear radiation effects of the tissues of the PLS on both sides. These effects can be responsible for the loss of tissue contrast on the scan. At the level of the ventricular bands (Fig. 3a) the scan again does not show evident pathology. Only a small difference in tissue density can be seen between the right and left side. The thyroid cartilage is intact and the PLS is of a low attenuation on both sides. The histologic examination indicates tumor infiltration in the anterior one-third of the right PLS (Fig. 3c, closed arrow). This finding can also be visualised by the macroscopic section (Fig. 3b, closed arrow), although the increased tissue density in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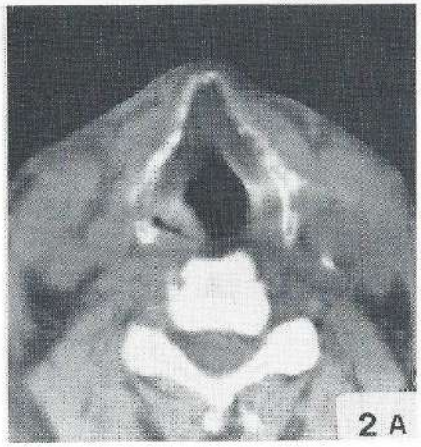
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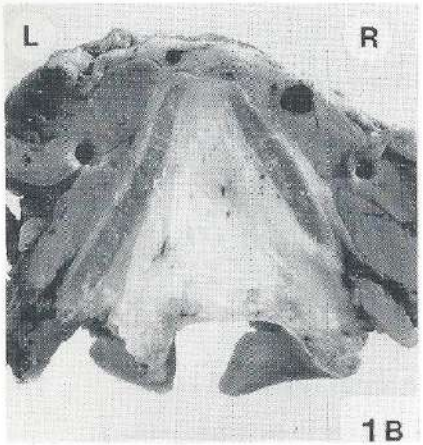
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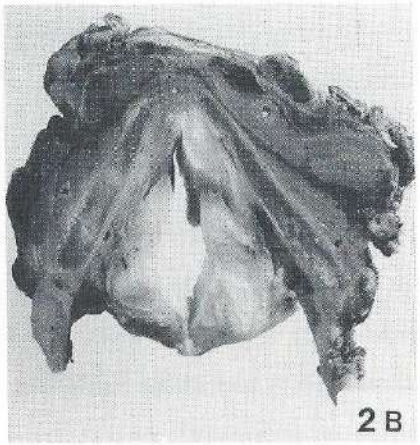
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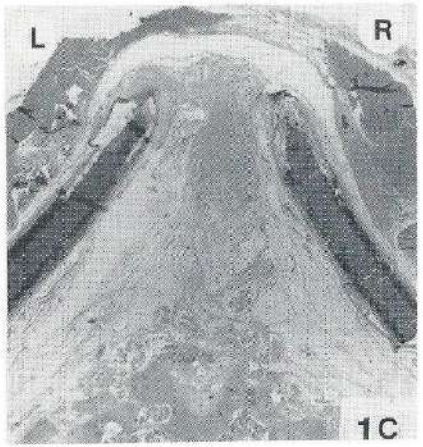
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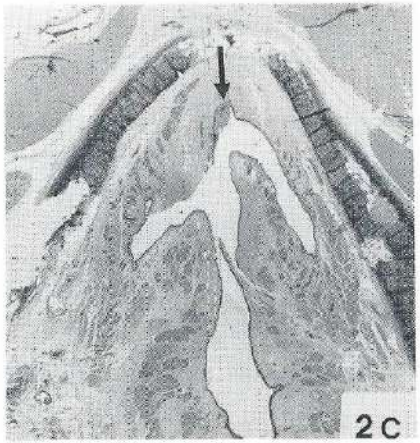
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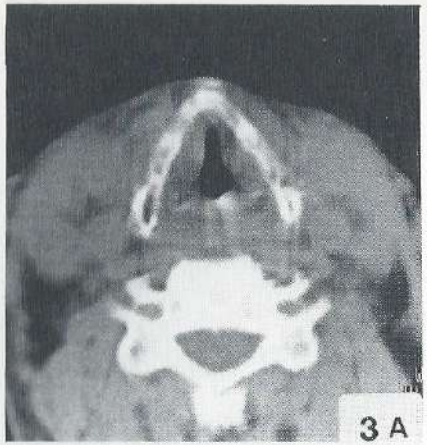
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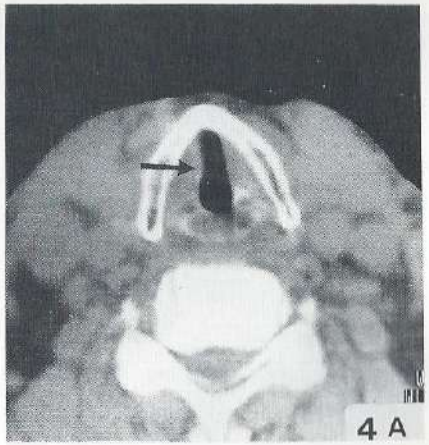
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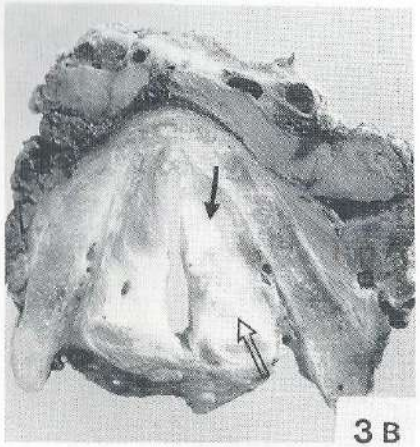
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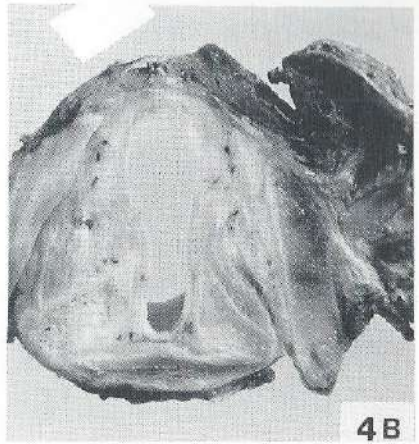
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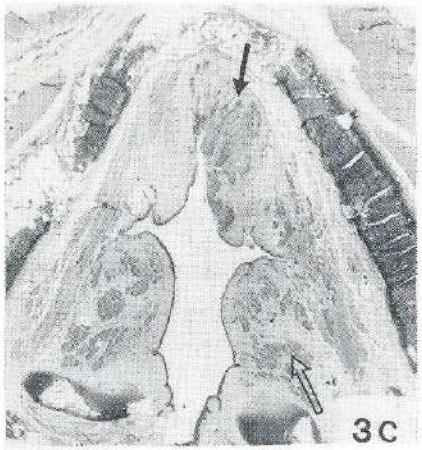
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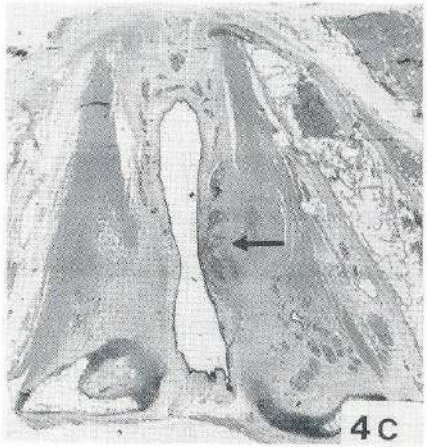
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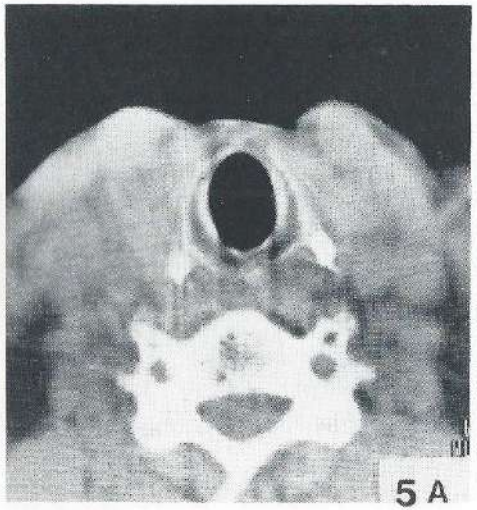

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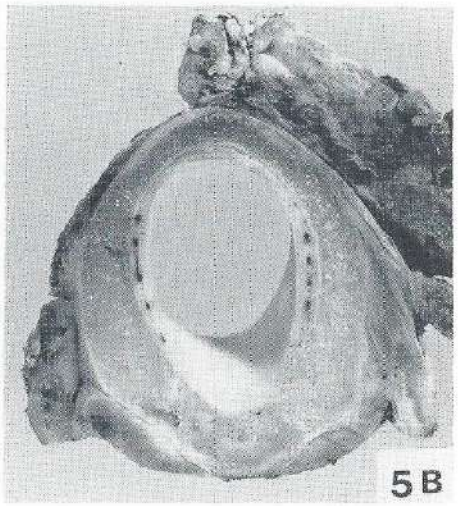

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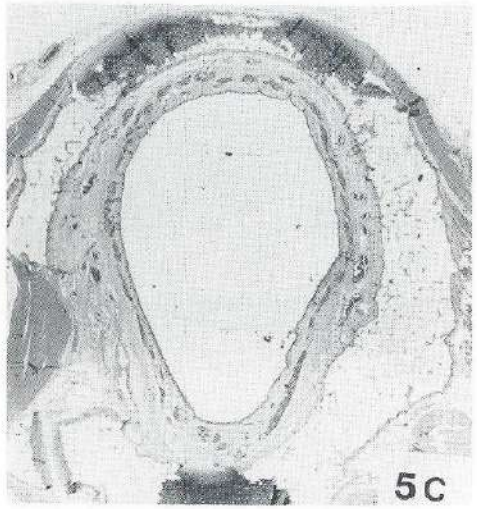


5C

this particular area can not be differentiated from the adjacent increased tissue densities in which radiation effects are present (Fig. 3b and 3c, open arrows).

At the glottic level small asymmetry of the PLS is visible on the scan (Fig. 4a, closed arrow). This abnormality is due to local

tumor recurrence or to edema. By microscopic examination the tumor was found on the right side (Fig. 4c).

At the high subglottic level pathology could no longer be detected either by means of CT scan, macroscopic or microscopic examination (Fig. 5a, 5b and 5c).

Comment

In case of a small recurrent lesion after radiotherapy, the CT scan can only confirm our clinical examination. As long as the cartilages are intact and it concerns only a small lesion, CT does not provide much additional information for the assessment of the localisation and extent of the tumor. In addition, in this case previous radiotherapy makes adequate visualisation more difficult. As will become apparent when we describe other cases the value of CT scan lies in its ability to assess more "remarkable" lesions, particularly before radiotherapy has taken place.

CASE II – A T_2N_0 glottic lesion

This case represents a patient, aged 72, with a T_2N_0 glottic lesion on the right side.

Clinical examination

Indirect and direct laryngoscopic findings include an ulcerative lesion of the right vocal cord with clear supraglottic and minor subglottic extension. The lesion could be interpreted as a transglottic lesion. Infiltration into the anterior commissure was also evident.

The left vocal cord revealed no pathology. Both piriform sinus looked completely normal. No suspect nodes were found in the neck. The lesion is represented by the drawing of Fig. II. The lesion could be staged clinically as a T_2N_0 glottic carcinoma after biopsies had proven to be positive. On the basis of the clinical and radiologic findings, including a CT scan on which destruction of the laryngeal skeleton was found, a total laryngectomy was performed.

CT and histologic examination

On CT scan, at the supraglottic level, we find tissue thickening and an increased density of the soft tissues in the anterior commissure region (Fig. 1a, closed arrow). This level is comparable with the histopathologic section represented by Fig. 1b. On this section tumor infiltration into the anterior commissure region is demonstrated clearly (Fig. 1b, closed arrow).

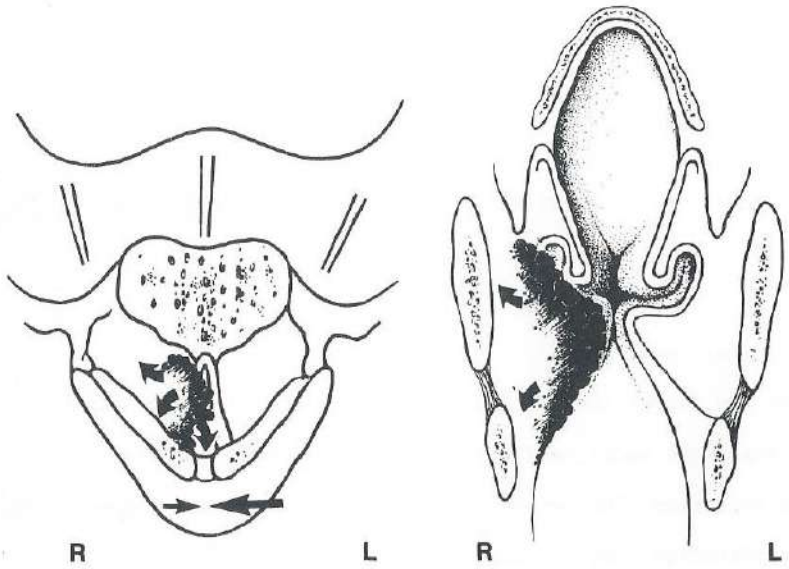
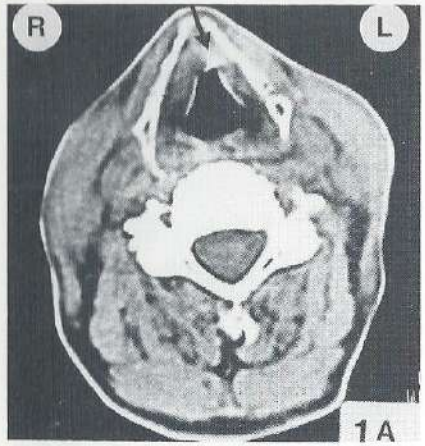
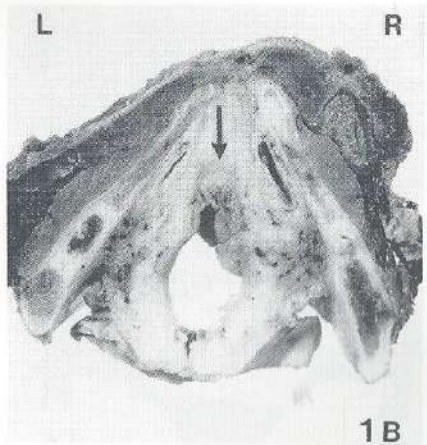
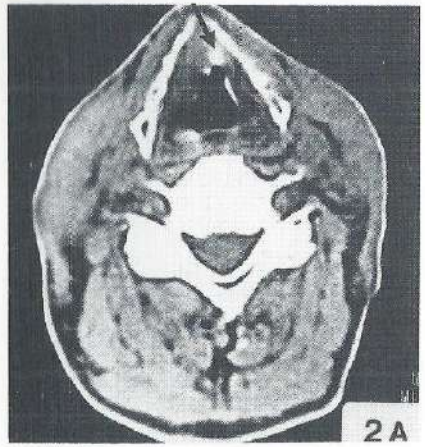
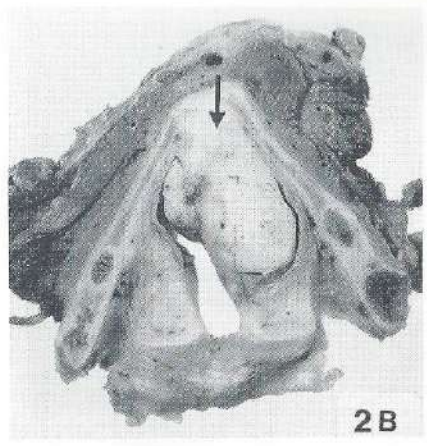


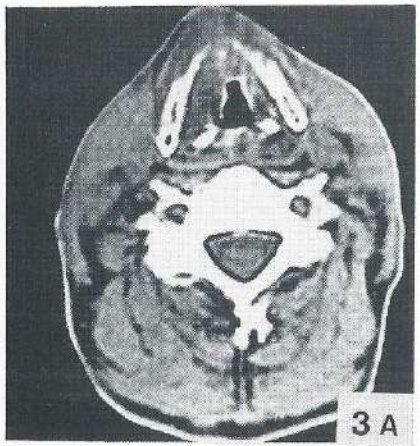
Fig. II

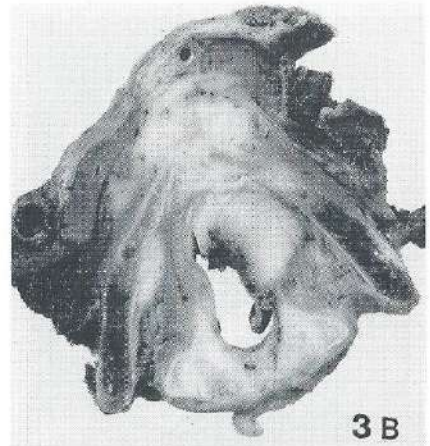


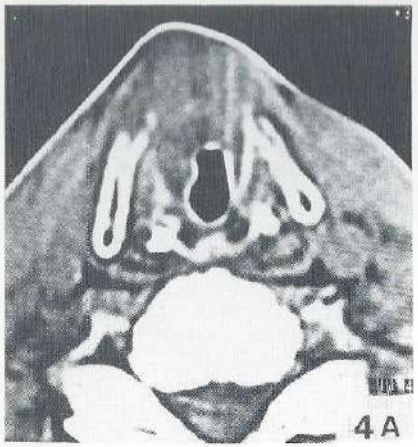




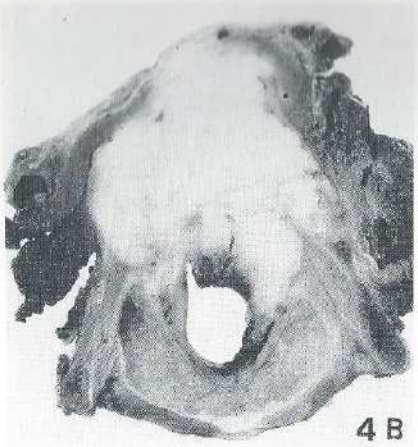




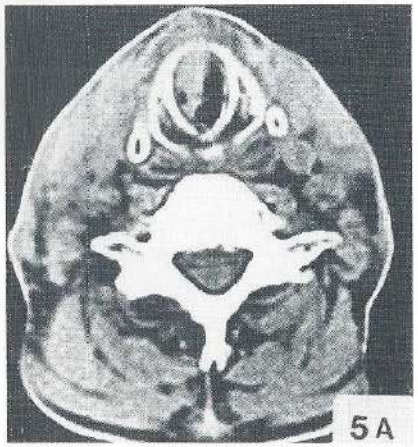




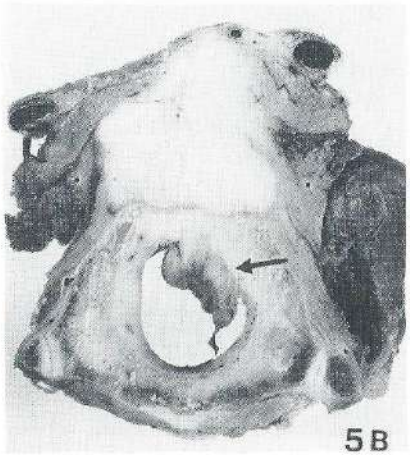
4A



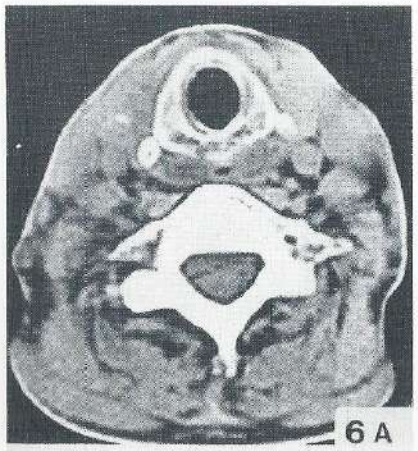
4B



5A



5B



6A

At the level of the ventricular bands asymmetry between the right and left side and increased density of the anterior commissure is present on CT scan (Fig. 2a, closed arrow). The asymmetry is probably due to tumor infiltration into the PLS, considering the corresponding histologic section (Fig. 2b).

At the level of the vocal cords it is definitely clear on the scan that severe infiltration into the anterior commissure with destruction of the thyroid cartilage and extralaryngeal tumor spread is present (Fig. 3a, 3b, 4a and 4b). At the high subglottic level clear subglottic tumor extension was found by laryngoscopy (Fig. 5b) and confirmed in the histopathologic sections. These findings seem to be in correspondence with the CT scan (Fig. 5a). At a lower level no pathology could be found (Fig. 6a).

Comment

Tumor extension, as found in this particular case, is not as rare as perhaps expected, considering our results and the results of others in the investigation of growth patterns of malignant laryngeal lesions. We should always be aware of the fact that direct and indirect laryngoscopic findings are based on abnormalities found in the intralaryngeal mucosal lining of the larynx. Fig. 3b clearly illustrates this diagnostic limitation. On this section, at the glottic level, a tumorous lesion is clearly visible on the right vocal cord with extension into the anterior commissure. The tumor infiltration into the anterior commissure was clearly underestimated by direct laryngoscopy. In addition Fig. 3b, 4b and 5b show extensive extralaryngeal tumor growth. This severe extralaryngeal extension

could not be detected, either by clinical or conventional radiologic examination, although some broadening of the larynx could be palpated shortly before operation. Nevertheless, it is clear from this case that CT adds a good deal of additional information. We therefore believe CT to be indispensable in the diagnostics of these growth patterns as demonstrated by this case report.

CASE III - A T_3N_1 glottic lesion

This case concerns a laryngeal carcinoma at the glottic level on the right side, in a male patient, aged 65.

Clinical examination

On direct and indirect laryngoscopy an ulcerative tumor of the right vocal cord with vocal cord fixation was seen. There seemed to

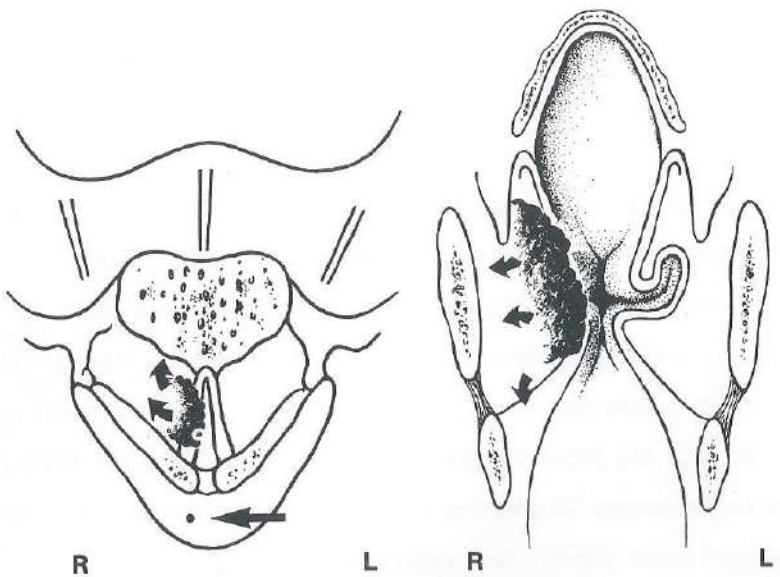


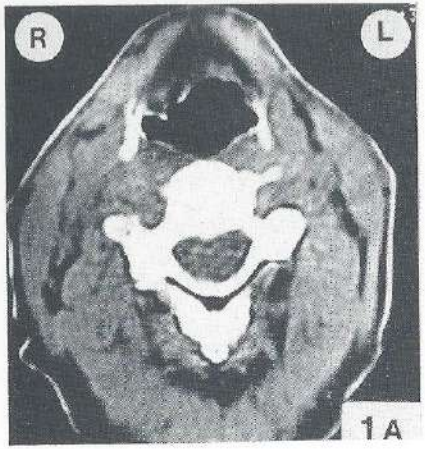
Fig. III

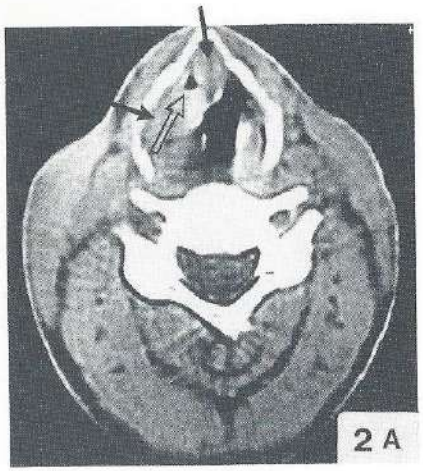
be intralaryngeal extension to the right ventricle and right ventricular band. The anterior commissure did not seem to be involved. The undersurface of the right vocal cord was also infiltrated by tumor (Fig. III). Although no evident subglottic extension was found, submucous infiltration could not be excluded. Extralaryngeal structures like the piriform sinus and valleculae were free of tumor. On the right side a subdigastric suspect node was palpable. Biopsies were positive for squamous cell carcinoma. Therefore, the lesion was classified as a T_3N_1 glottic lesion on the right side.

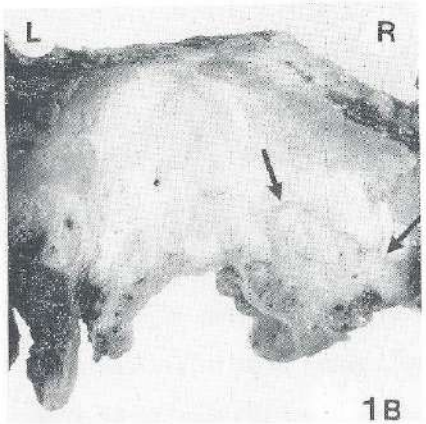
CT and histologic examination

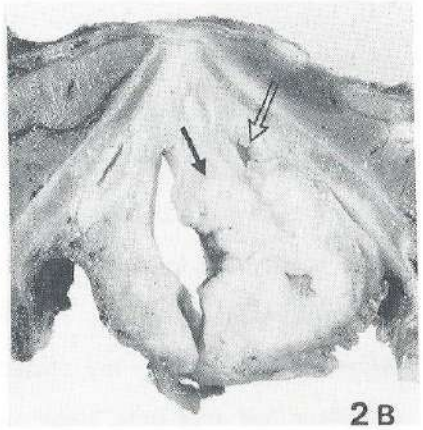
At the high supraglottic level on CT scan (Fig. 1a) slight asymmetry of the contour of the epiglottis is visible, probably due to minor infiltration into the PES, although the fibrofatty tissue of the PES is of a very low attenuation. The macroscopic examination indicates PES involvement (Fig. 1b, closed arrows). This finding is confirmed microscopically (Fig. 1c, closed arrow). Apart from this clearly circumscribed area with tumor involvement, the PES seems to be free of tumor.

At the level of the ventricular bands asymmetry is clearly visible due to tumor infiltration of the PLS on the right side (Fig. 2a, closed arrows). There also seems to be a tissue thickening of the anterior commissure. The laryngeal skeleton appears to be intact on the scan at this level. A small air-filled lucency is seen representing the sacculus of the laryngeal ventricle (Fig. 2a, open arrow). The macroscopic findings (Fig. 2b) correlate with the CT scan.


R
L
1A


2A


L
R
1B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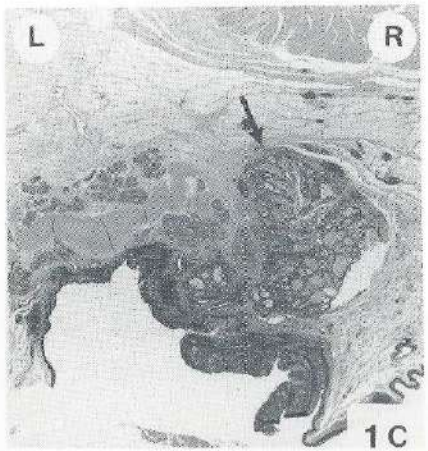
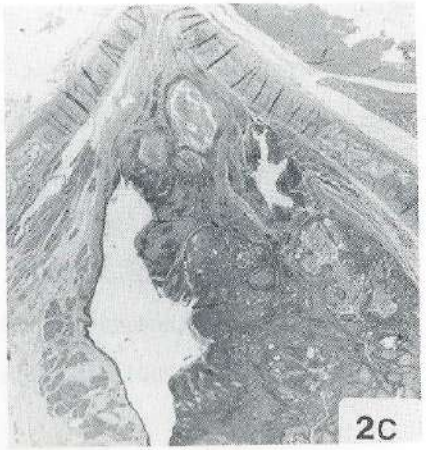
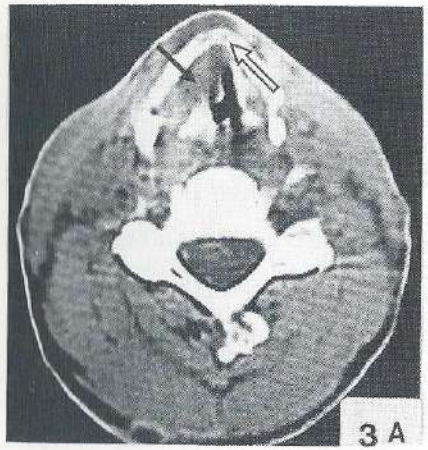
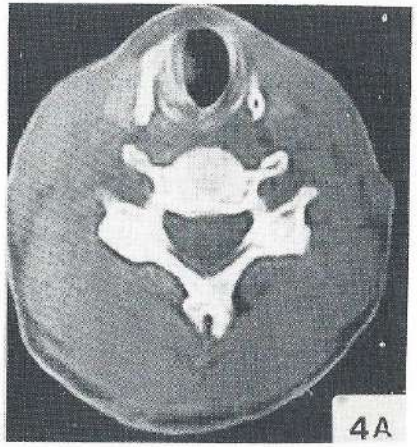
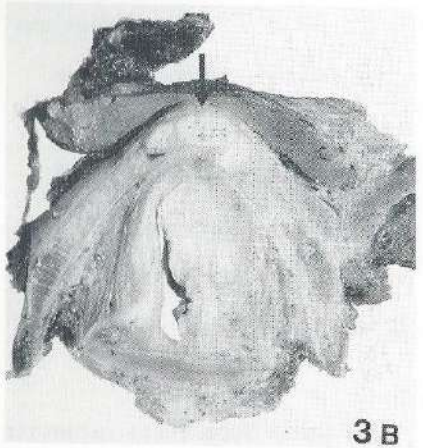

L
R
1C


2C


3A


4A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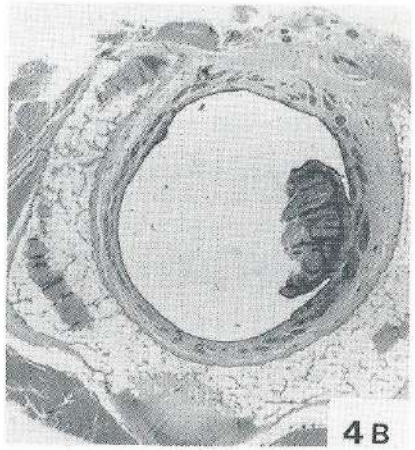
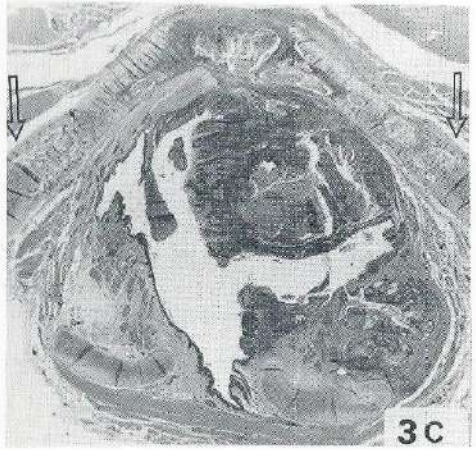

4B


3C

Note the bulk of the tumor infiltrating the PLS (Fig. 2b, closed arrow). The open arrow indicates the sacculus of the laryngeal ventricle. Infiltration into the anterior commissure can not be demonstrated on the macroscopic section. The microscopic section shows that the tumor surrounds the sacculus of the ventricle (Fig. 2c) and infiltrates into the anterior commissure region. The laryngeal skeleton is left intact. The PLS is completely infiltrated.

At the glottic level infiltration of the PLS is still present and asymmetry of both PLS is clearly visible on CT scan (Fig. 3a, closed arrow). The laryngeal framework seems to be intact. Slight variations in density of the thyroid cartilage in the anterior commissure can not be regarded as pathologic on CT scan (Fig. 3a, open arrow). Nevertheless, involvement of the thyroid cartilage is seen on both macroscopic and microscopic sections (Fig. 3b, closed arrow, and Fig. 3c). The tumor seems to spread into both alae of the thyroid cartilage in lateral direction as far as the open arrows indicate (Fig. 3c).

At the high subglottic level (Fig. 4a) a small subglottic extension is demonstrated and directly confirmed by the microscopic section (Fig. 4b). The cricoid is left intact.

Comment

It is clear that CT did not demonstrate tumor infiltration into the thyroid cartilage of the anterior commissure. The histologic sections, however, did demonstrate this infiltration. Only slight variations in density of the cartilage are visible on the scan. These variations, however, are not to be considered directly as abnormal

due to the fact that the amount of calcification in a non-pathologic thyroid cartilage can also vary considerably. We therefore feel that demonstration of cartilage invasion on the scan depends first on the tumor volume, infiltrating the cartilage. In fact, a larger tumor mass will be visualised more clearly on the scan (compare case 2). Second, the modes of calcification of the thyroid cartilages are of utmost importance. Tumorous tissue can not be differentiated from adjacent calcified cartilage, if both tissues represent the same tissue density. These findings support a general consensus that CT is particularly indicative of tumor infiltration into the cartilage, when evident cartilage destruction is found.

Case IV - A T_1N_0 supraglottic lesion

This case represents a small supraglottic lesion of a man, aged 53.

Clinical examination

The lesion was found on the laryngeal surface of the epiglottis on the left side, with macroscopic extension to the ary-epiglottic fold on the left. The lesion was confined to the supraglottis. Indirect laryngoscopy revealed no abnormalities at the glottic level. The vocal cord mobility was completely normal. The tip of the epiglottis, the valleculae and the base of the tongue were free of tumor. No pathologic nodes were found in the neck. The extent of the lesion is demonstrated by Fig. IV. Biopsies were positive for squamous cell carcinoma. The lesion could be classified as a T_1N_0 supraglottic carcinoma. A supraglottic laryngectomy was performed.

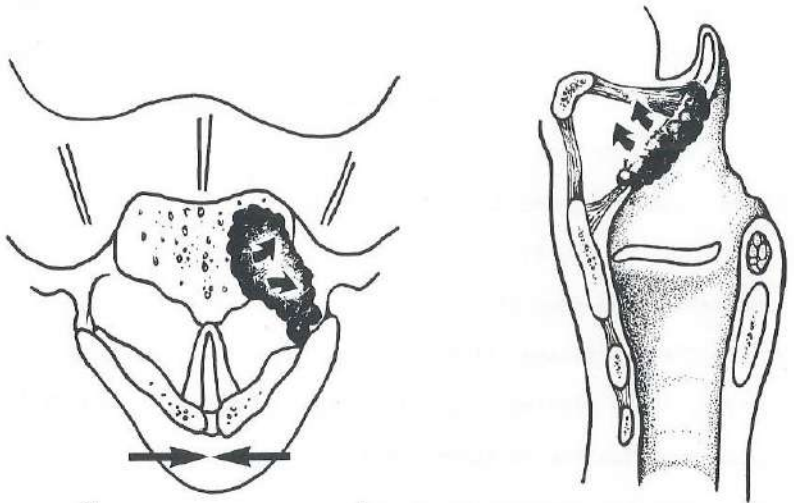
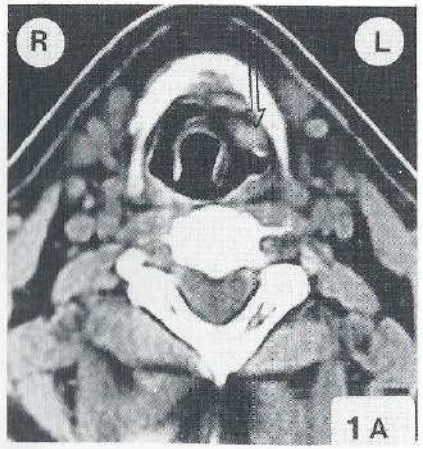


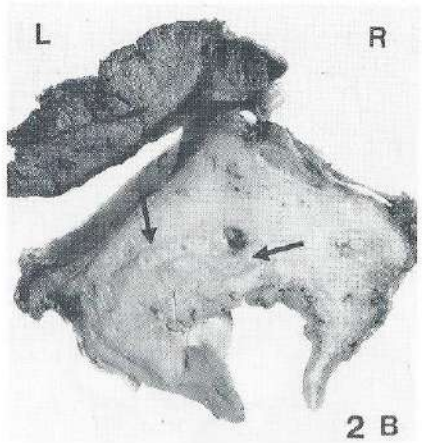
Fig. IV

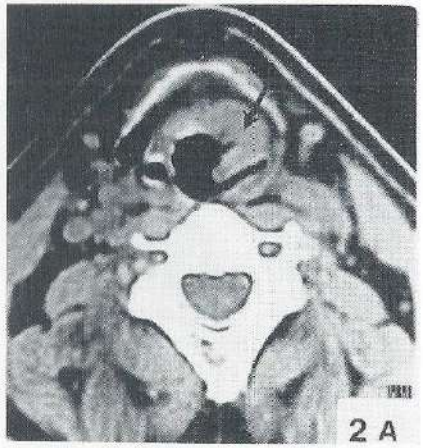
CT and histologic examination

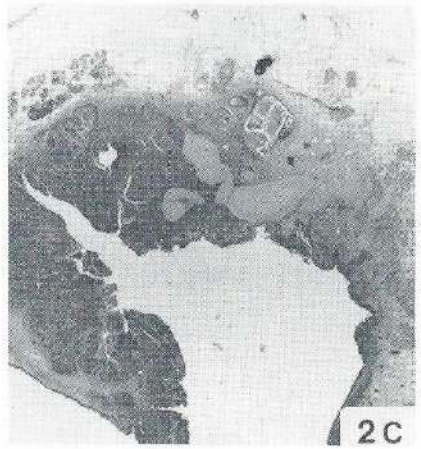
On CT scan asymmetry of the valleculae is present due to submucous tumor infiltration or edema on the left side (Fig. 1a, open arrow). On the next slice, tumor infiltration into the PES, particularly on the left is clearly visible (Fig. 2a, closed arrow). This finding is comparable with the histologic section of Fig. 2b and is illustrated microscopically by Fig. 2c. The tumor clearly infiltrates the PES as far as indicated by the closed arrows of Fig. 2b. A detail shows the destruction of the cartilage (Fig. 2d, closed arrow).

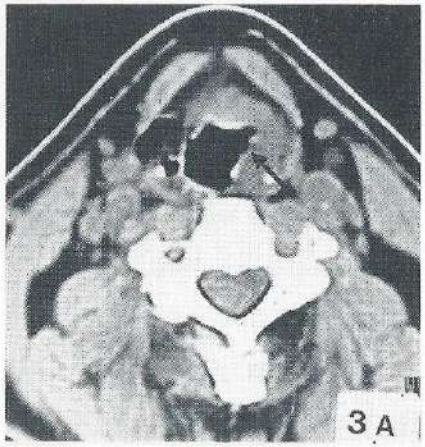
On the next slice (Fig. 3a) the scan again clearly shows tumor infiltration into the PES with thickening of the ary-epiglottic fold on the left side. The contour of the epiglottis seems to be disturbed markedly (Fig. 3a, closed arrow), due to submucous tumor extension and cartilage destruction.

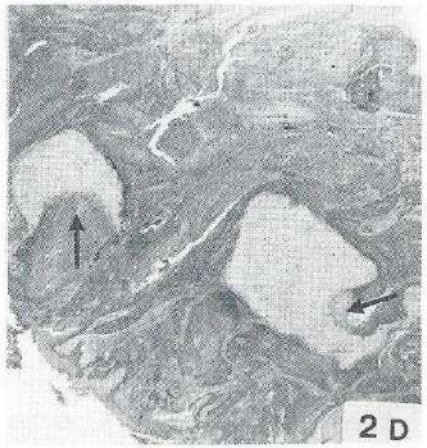


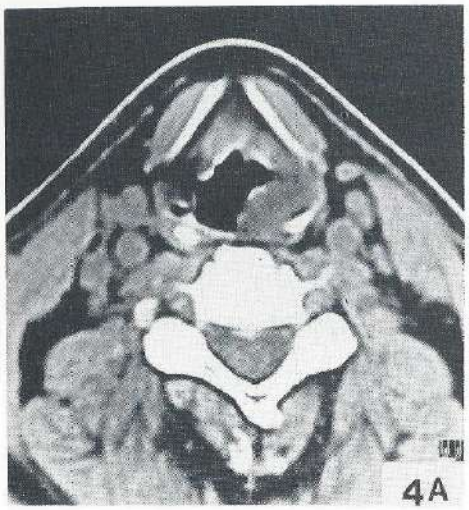


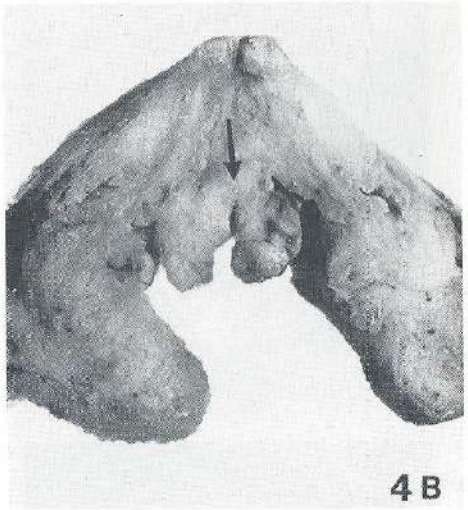


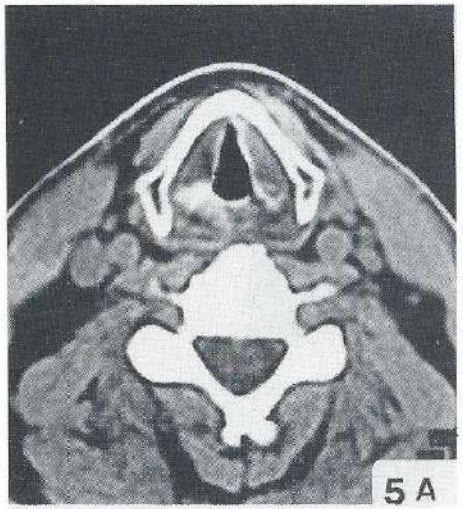


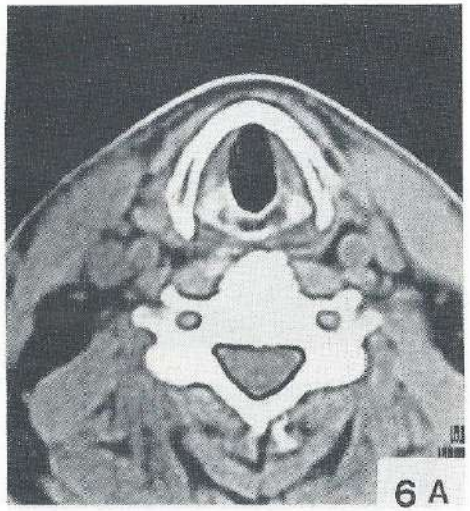












At a lower level, the level of the ventricular bands, asymmetry is recognised on CT scan in the anterior commissure (Fig. 4a) whereas the histologic section shows tumor invasion into the anterior commissure region (Fig. 4b, closed arrow). At the glottic level and high subglottic level no abnormalities are seen (Fig. 5a and 6a).

Comment

We may presume that CT clearly demonstrated the invasion into the PES. The laryngeal cartilages were intact. Only the cartilage of the epiglottis seemed to be destructed. This was confirmed by the histologic examination. A tumor originating on the laryngeal surface of the epiglottis can invade the PES through the orifices cribiformes. This represents a route of less resistance. In this case, however, the cartilage of the epiglottis was also partly destructed. According to the images of the various scan sections we feel CT to be very sensitive to demonstrate tumor invasion into the PES.

CASE V - A T_2N_1 supraglottic lesion

In this case a more extensive supraglottic tumor growth is presented by a large supraglottic lesion in a man, aged 50.

Clinical examination

Indirect and direct laryngoscopy revealed a tumor on the laryngeal surface of the epiglottis. At the high supraglottic level only some irregularity and some slight ulceration of the mucosa were visible on the laryngeal surface of the epiglottis. At the lower supraglottic level the laryngeal surface of the epiglottis was completely ulcerative. The lesion extended to both ventricular bands. The right ventricular band was ulcerative. The left ventricular band only presented submucous tumor extension. Both ventricles were infiltrated by tumor tissue. Due to the severe ulceration and submucous extension of the lesion, particularly on the laryngeal surface of the epiglottis,

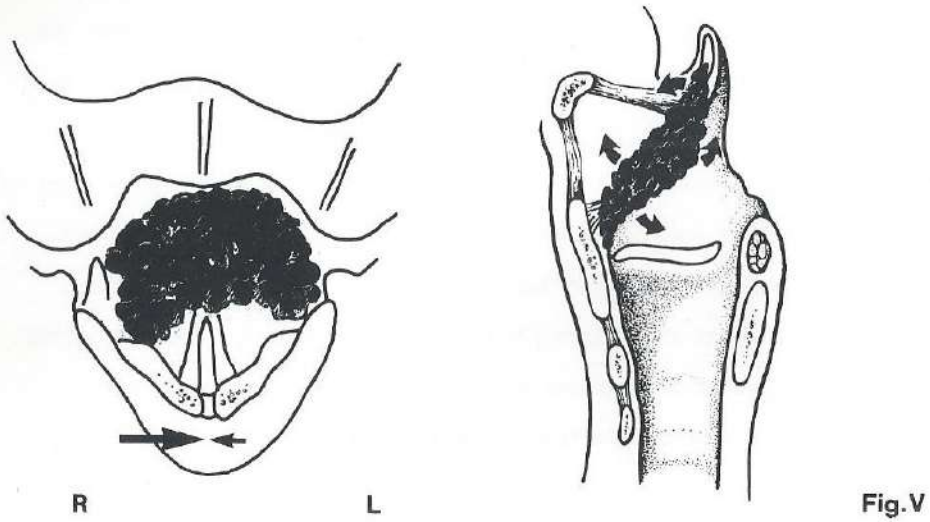


Fig.V

infiltration into the PES was very likely to be the case. The valleculae and base of tongue seemed to be free of tumor. The severe extent of the lesion is presented by Fig. V. Both vocal cords seemed to be free of tumor. The lesion, however, did infiltrate the anterior commissure at the glottic level. Decreased mobility of the left vocal cord was found on indirect laryngoscopy. In the neck at the sub-digastric level on the right side a suspect node was palpable. The lesion was clinically classified as a T_2N_1 supraglottic carcinoma. Again, biopsies were positive for squamous cell carcinoma. Due to the tumor extension and the suspect palpable node in the neck a total laryngectomy was performed, combined with a neck dissection on the right side.

CT and histologic examination

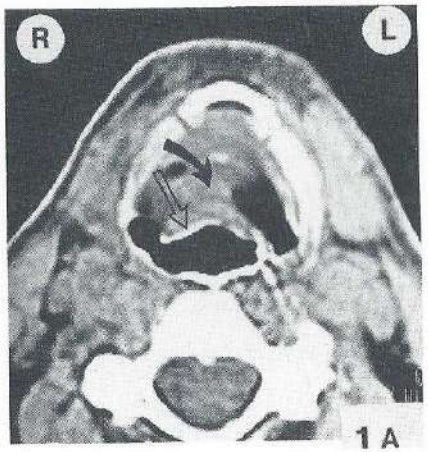
At the high supraglottic level asymmetry of the valleculae is clearly

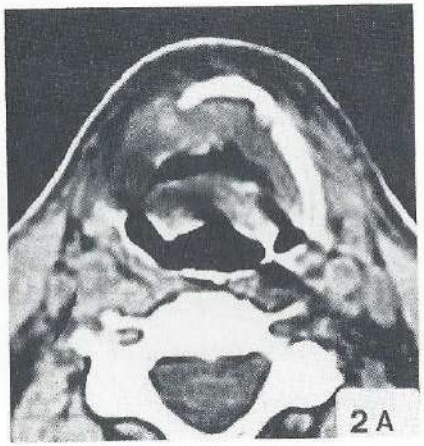
demonstrated on CT scan with tumor infiltration into the PES (Fig. 1a, closed curved arrow). The hyoid bone seems to be intact. Note the contour of the laryngeal surface of the epiglottis is still intact (Fig. 1a, open arrow), but the epiglottis is pressed in a posterior direction by a tumorous mass. This corresponds with the histopathologic section (Fig. 1c). The tumor infiltrates the PES clearly. The cartilage of the epiglottis is probably destructed at a lower level.

On the next slice, clear infiltration into the PES is found with a central lucency (Fig. 2a). The laryngeal surface of the epiglottis is also destructed. On the corresponding histopathologic section we found tumor necrosis into the PES (Fig. 2b). The cartilage of the epiglottis seemed to be partly destructed (Fig. 2c, closed arrow).

On the next scan levels one can see that the lesion extends into the laryngeal lumen as diagnosed by direct laryngoscopy and infiltrates the thyroid cartilages by severe, almost total destruction, as demonstrated by Fig. 3a and 4a. Note that the piriform sinus is obliterated on the right side (Fig. 4a, closed arrow). This finding is probably a result of tumor infiltration and thickening of the ary-epiglottic fold. Fig. 4a shows the cartilage to be infiltrated at several places and tumor extension outside the cartilage is very likely to be present. These findings correlate with the histo-pathologic findings illustrated by Fig. 4b and 4c.

On the next scan level, probably the level of the ventricles (Fig. 5a), cartilage destruction is again clearly demonstrated. On the corresponding histologic section, particularly on the left side, a dense tumor mass is visible (Fig. 5b and 5c). This mass is not


R
L
1A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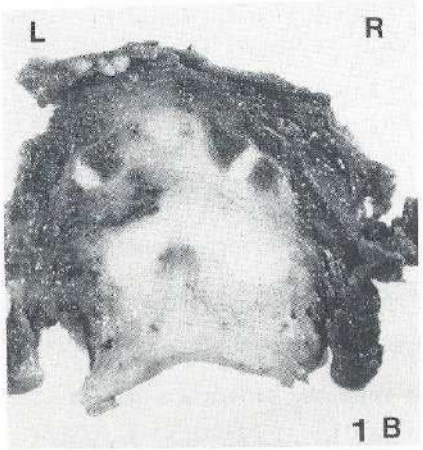
L
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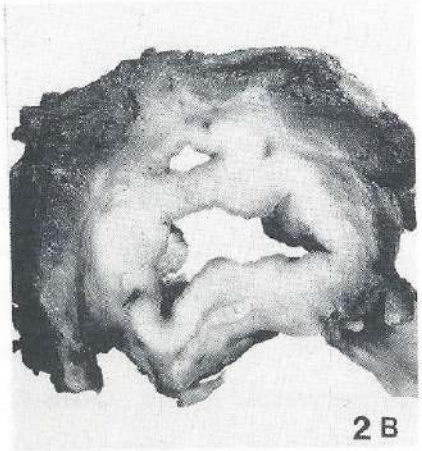
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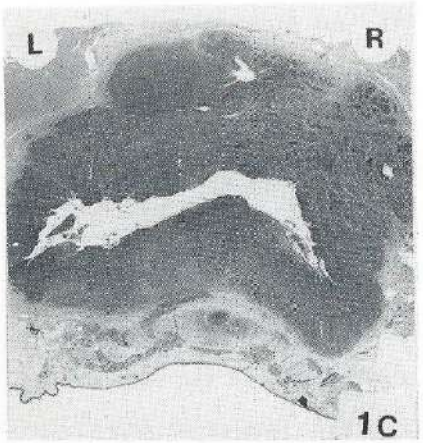
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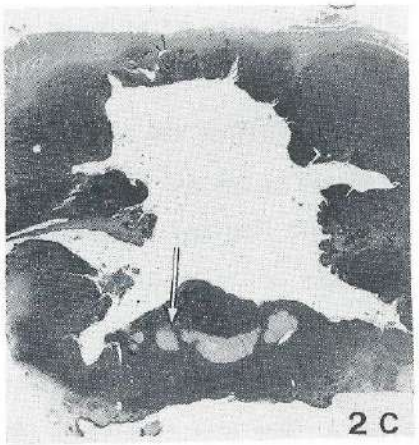
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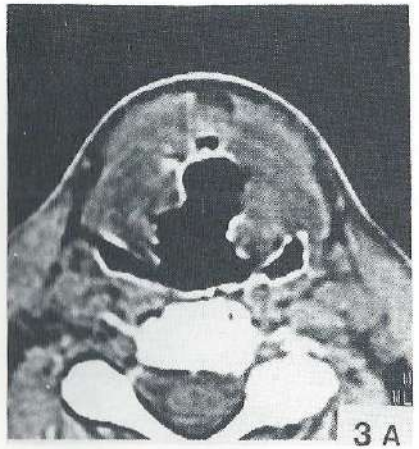
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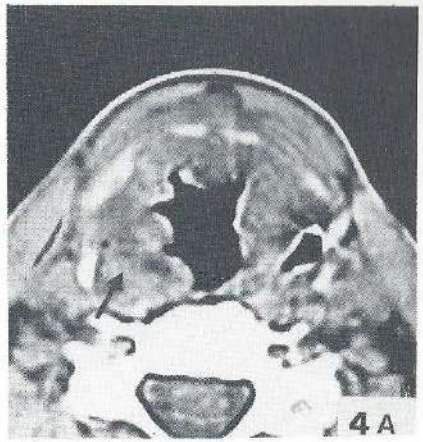
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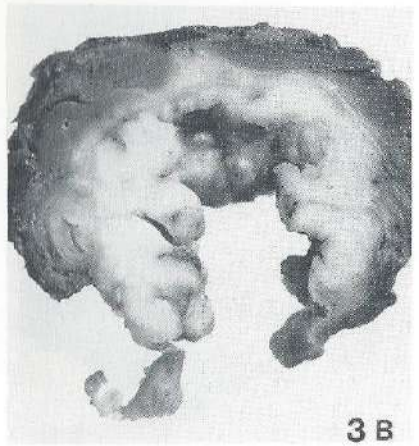
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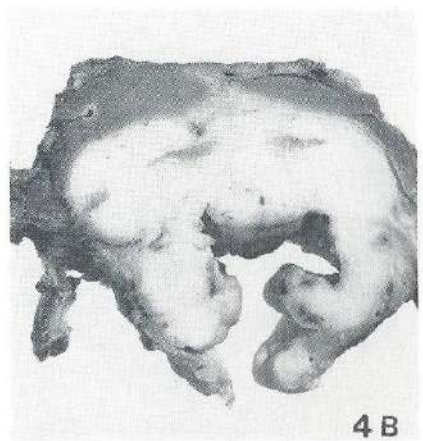
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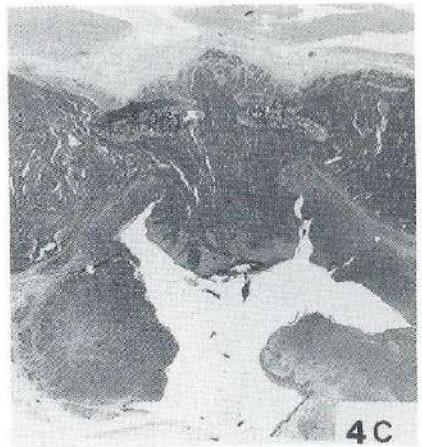
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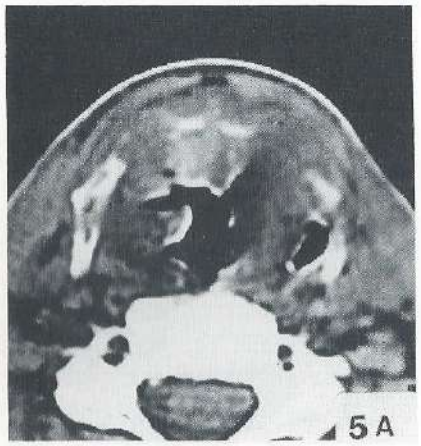
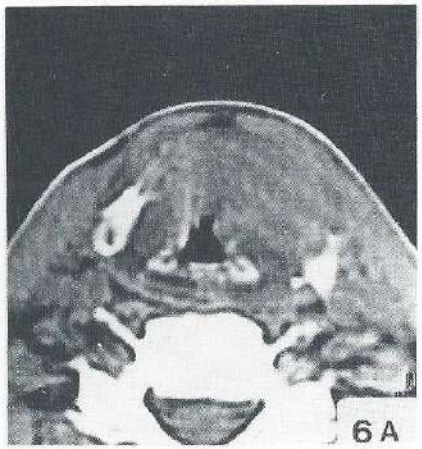
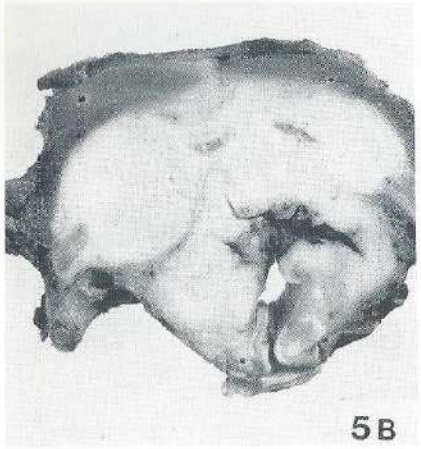
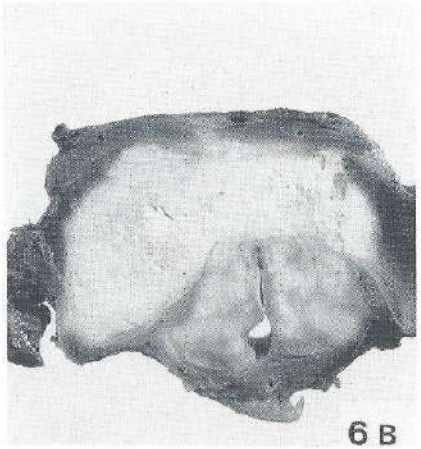
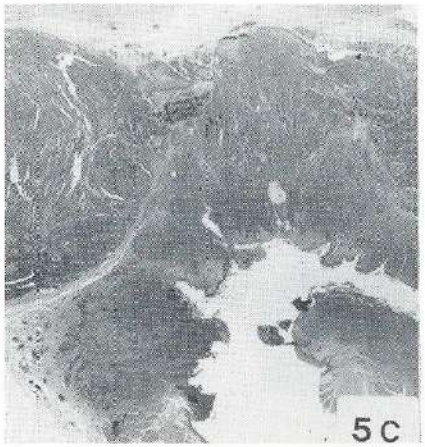
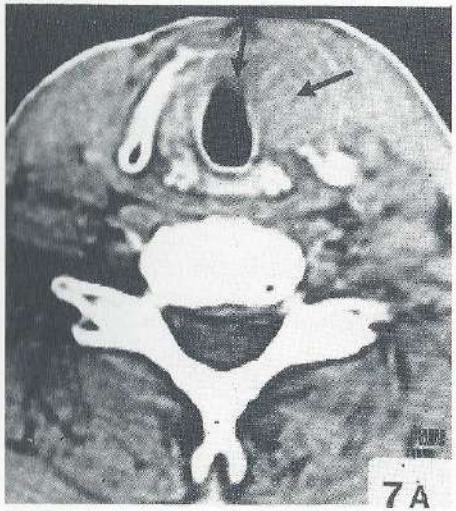


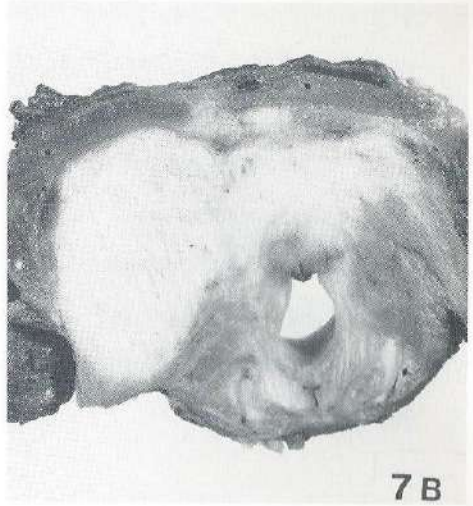












precisely delineated on CT scan. Fig. 6a shows the thyroid cartilage to be almost completely destructed. Note the invasion of tumor into the PLS on both sides and the severe tumor mass outside the laryngeal framework (Fig. 6b).

At the glottic level, the posterior two-third of both true vocal cords seemed to be normal. CT scan reveals an incomplete laryngeal framework and asymmetry in the anterior commissure and infiltration into the PLS on both sides (Fig. 7a, the closed arrows indicate the invasion in the PLS and anterior commissure). Fig. 7b again, shows tumor infiltration into the anterior commissure and a large tumor mass on the left side.

Comment

It is clear that the CT scan demonstrated a remarkable cartilage destruction and extralaryngeal tumor growth. This growth pattern was not diagnosed by clinical and conventional radiologic examination.

Clinical examination showed tumor extension into the anterior commissure and suggested tumor infiltration into the PLS, on the left side, due to the fact that decreased mobility of the left vocal cord was found. The infiltration at the glottic level as demonstrated by Fig. 6b and 7b was not presumed. It is a remarkable fact that only decreased mobility of the left vocal cord was found and not total fixation. In this case CT completed the clinical findings. CT was furthermore very illustrative in the demonstration of tumor, infiltrating the PES and both PLS.

CASE VI - A T_2N_1 subglottic lesion

Within this series of illustrations it seems to be worthwhile to demonstrate a case with subglottic tumor involvement. Such a lesion can be presented by a glottic carcinoma with a remarkable subglottic extension.

Clinical examination

Our patient, a woman, aged 65, was found to have on laryngoscopy a tumorous lesion at the glottic level. The tumor was found in the anterior commissure region and on both vocal cords. Only the posterior one-third of both cords seemed to be free of tumor. The process did not extend to the supraglottic level. Decreased mobility, but not total fixation, of both cords was found. At the subglottic level a marked tumor extension was also found. The growth of the subglottic tumor mass was almost circular. The laryngeal lumen was narrowed. Destruction of the crico-thyroid membrane was presumed. However,

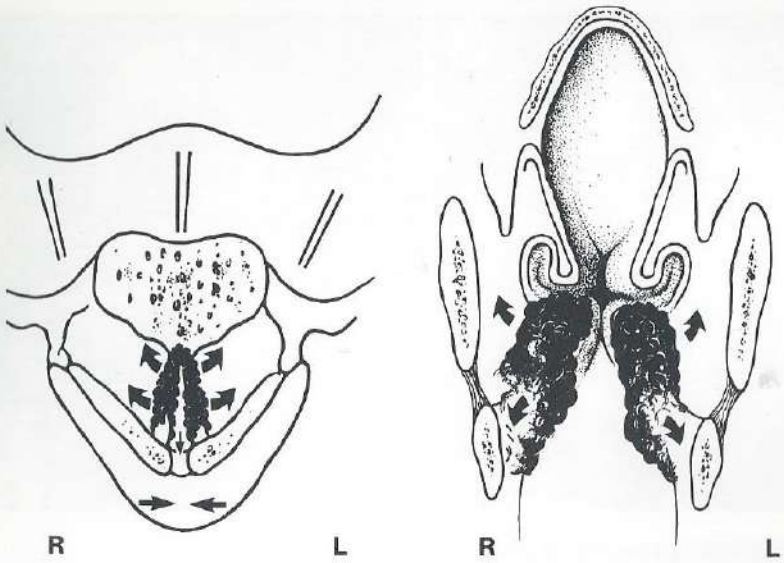


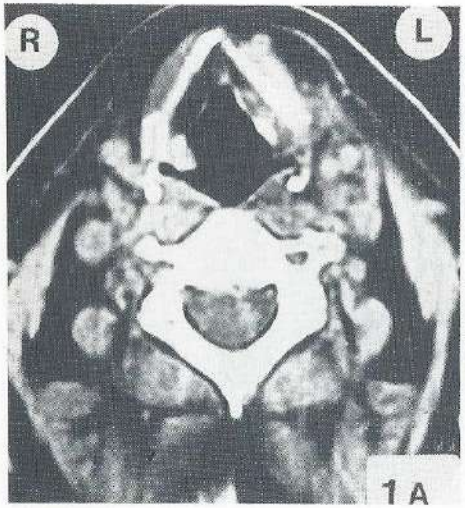
Fig. VI

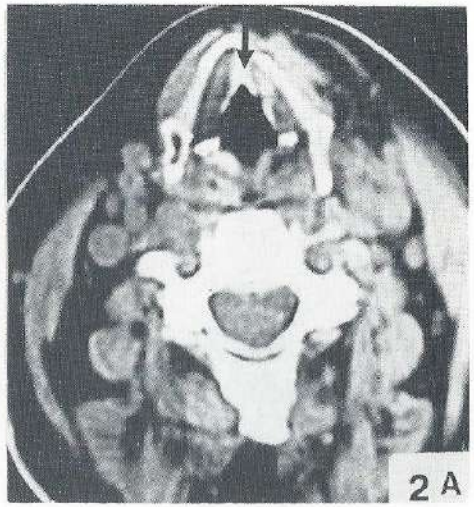
pretracheal tumor involvement did not seem to be the case. Pretracheal nodes could not be palpated. On the contrary, a suspect group of mobile nodes with a diameter of approximately 4 cm was palpated on the left side in the neck, in the mid-jugular region. The lesion was classified as a T_2N_1 subglottic lesion. The extension of the lesion is presented by Fig. VI.

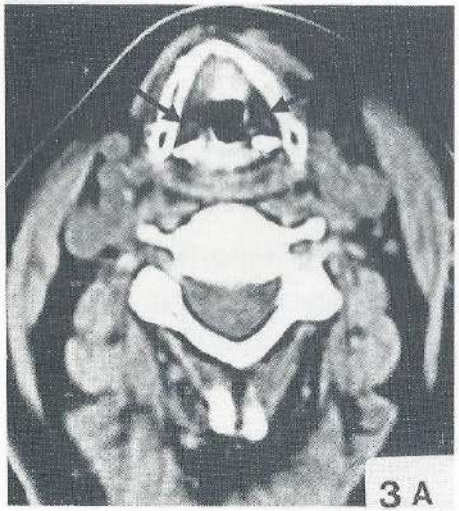
CT and histologic examination

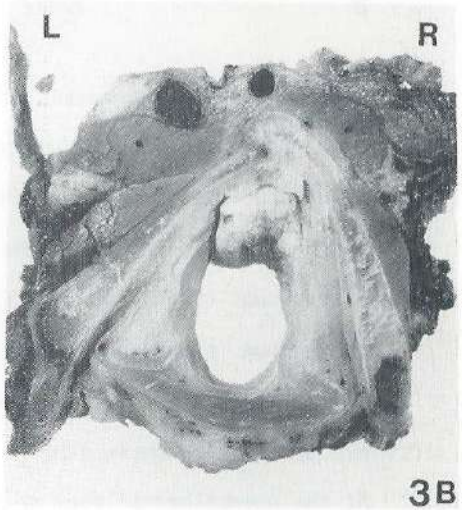
At the supraglottic level no abnormalities were seen on CT scan (Fig. 1a). The PLS seems to be of a low tissue density and the thyroid cartilage is intact. At a lower level the arytenoids are demonstrated and an increased density, probably due to tumor involvement in the anterior commissure, is visible (Fig. 2a, closed arrow).

At the glottic level (Fig. 3a) this finding is clearly demonstrated. Tumor involvement is seen as a thickening of the anterior commissure

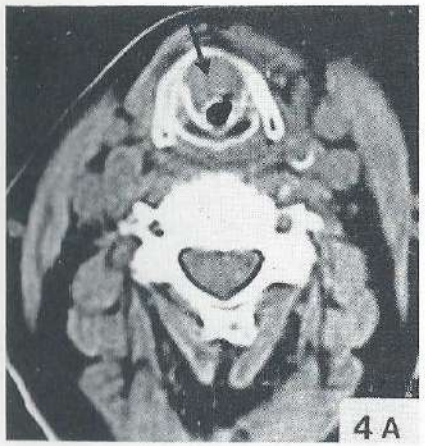


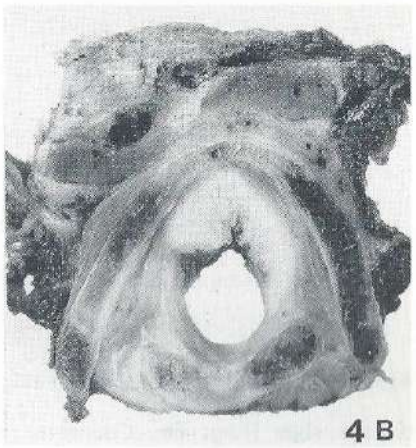


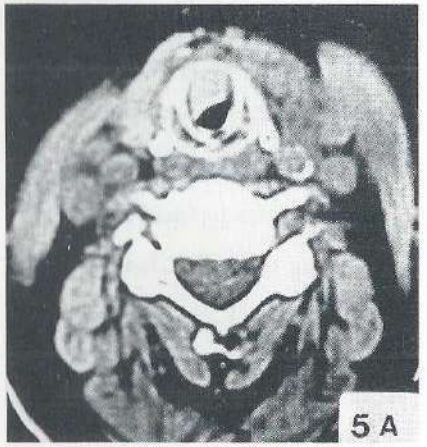


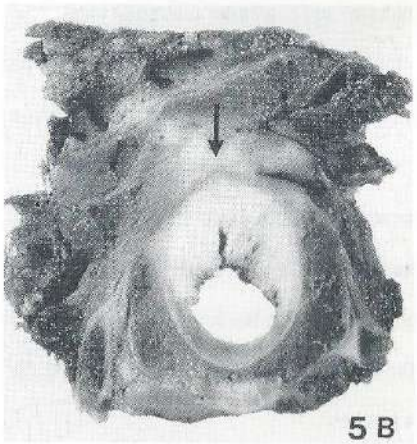


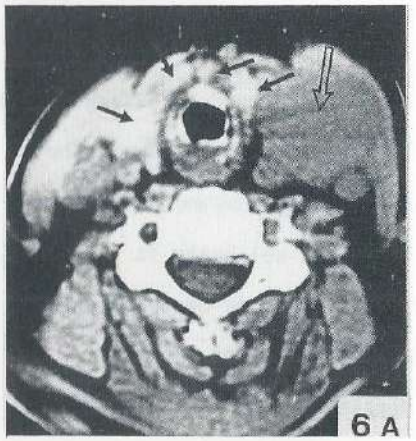
on CT scan. The posterior part of both PLS seems to be free of tumor, as a normal tissue density is found on CT scan (Fig. 3a, closed arrows) The thyroid cartilage is intact. The section corresponds well with the histologic section (Fig. 3b). Cartilage destruction was found neither macroscopically nor microscopically.

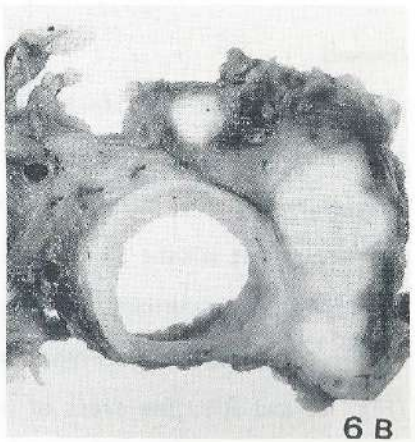












At the high subglottic level tumor extension into the anterior commissure is clearly visible on the scan (Fig. 4a, closed arrow). The thyroid cartilage is still intact as is demonstrated by Fig. 4b. On CT scan no clear destruction of the crico-thyroid membrane can be visualised (Fig. 5a). The destruction of the membrane, however, is definitely found on the histologic section (Fig.5b, closed arrow).

At the level of complete closure of the cricoid ring, small high density zones are visible anterior and lateral to the cricoid ring on the scan (Fig. 6a, closed arrows). These densities proved to be pathologic after histopathologic examination (Fig. 6b). We therefore should be aware of these abnormalities, represented by zones of higher density in this region on the scan, particularly when the crico-thyroid membrane is very likely to be infiltrated. This last scan section also reveals some information about the palpable nodal mass in the neck on the left side (Fig. 6a, open arrow). Clear asymmetry between the left and right side of the neck is present. On the scan the mass seems to be of equal density as the adjacent tissues.

Comment

It can be concluded that the scan provides a good deal of additional information about the infiltration of the process into the anterior commissure and its subglottic extension. Although the extralaryngeal growth was not missed by CT, the scan could not delineate it precisely. The histologic examination, however, clearly revealed destruction of the crico-thyroid membrane and extralaryngeal tumor growth (Fig. 5b and 6b). The areas of higher density on the scan were only

suspected to be pathologic. Without a histologic verification such findings can only be interpreted as abnormal. The diameter of the nodal mass in the neck on the left side could not be measured exactly on the scan. Contrast enhancement might have been helpful but was not carried out in this case.

CASE VII - A piriform sinus lesion

Since lesions arising from the medial wall of the piriform sinus can infiltrate the PLS easily and because they can even grow into the laryngeal lumen, it seems to be worthwhile to investigate the growth pattern of such a piriform sinus lesion and its demonstration on CT scan.

Clinical examination

In this case the laryngoscopic findings demonstrated an ulcerative lesion of the right piriform sinus of a man, aged 50. The piriform sinus was completely destructed and the lesion seemed to infiltrate into the lateral pharyngeal wall. The base of tongue felt normal on palpation. Edema of the right vallecula was present. At the supra-glottic level severe intralaryngeal edema was also found on the right side. The mucosa of both arytenoids and both vocal cords were free of tumor. No intralaryngeal ulceration was present. Submucous intralaryngeal tumor growth and spread was probably the case. Fixation of the vocal cord on the right side seemed to be a result of tumor infiltration into the PLS. The exact delineation of infiltration could not be established by conventional diagnostic

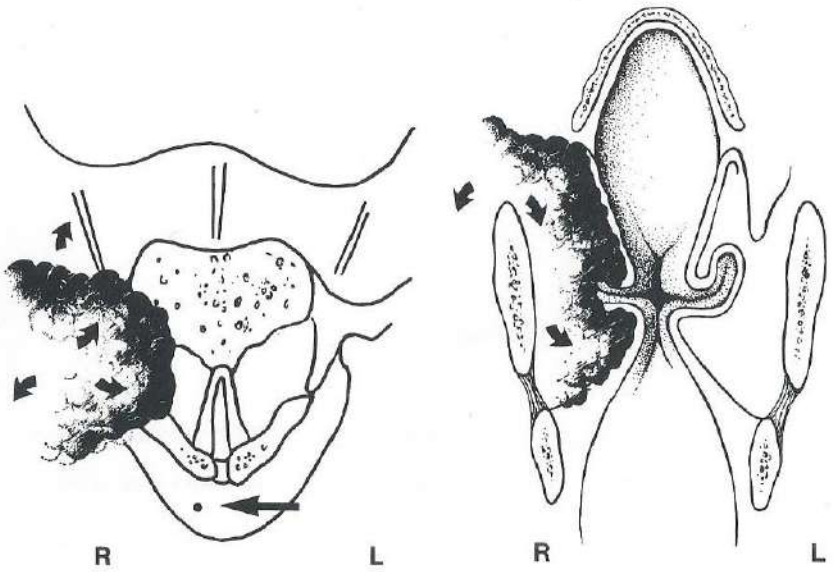


Fig. VII

methods. In the neck, on the right side, a large nodal mass of approximately 4 cm in diameter could be palpated. Fig. VII demonstrates this large tumorous lesion and the probable intralaryngeal submucous extension. Biopsies were positive for squamous cell carcinoma. A laryngo-pharyngectomy was performed with an en bloc neck dissection on the right side.

CT and histologic examination

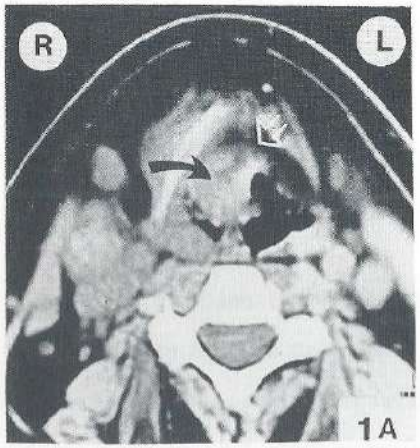
On the scan at the high supraglottic level, a large mass is visible with a central lucency (Fig. 1a, closed curved arrow). The mass seems to extend into the PES as far as the open arrow indicates. The contour of the epiglottis is disturbed. Clear asymmetry of the laryngeal structures can be seen. The scan level is in correspondence with the histologic section, presented by Fig. 1b

and 1c. The open arrows on both figures indicate the extension of the tumorous lesion, while the closed arrows indicate the contour of the epiglottis which is partly destructed. A large tumor mass is seen on this section and cartilage destruction is demonstrated.

At a lower level complete disturbance of the contour of the PLS is seen on the scan, due to a large tumor mass with an extensive growth around the right ala of the thyroid cartilage with destruction of the cartilage (Fig. 2a, closed curved arrow). Evident thickening of the PLS can be seen (Fig. 2a, open curved arrow). The tumor mass appears to infiltrate into the PLS. Further there is evidence of central necrosis. On CT scan, the palpable mass on the right side is clearly demonstrated.

At the level of the ventricular bands destruction of the thyroid cartilage is almost complete on the right side (Fig. 3a, 3b). This is demonstrated again on the next scan level (Fig. 4a). Due to tumor growth and infiltration, destruction of the vocal process of the arytenoid on the right side is found. Fig. 4c illustrates how the tumorous mass replaced the lower part of the right thyroid ala and the vocal process of the arytenoid.

At the high subglottic level asymmetry of the intralaryngeal lumen can be seen on the scan. No exact tumor infiltration into the cricoid ring can be visualised, due to the fact that the cricoid ring and the tumor seem to be of equal density (Fig. 5a). On the macroscopic section the cricoid ring appears to be intact, although the tumor mass is very near to the ring (Fig. 5b, closed arrow). The microscopic section similarly, illustrates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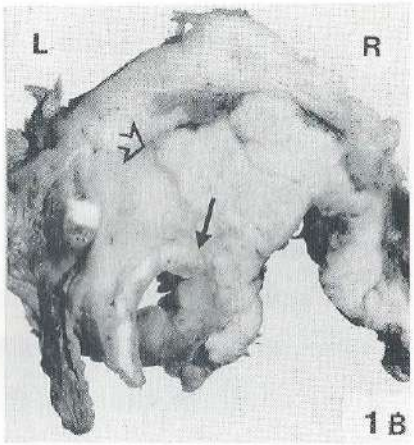
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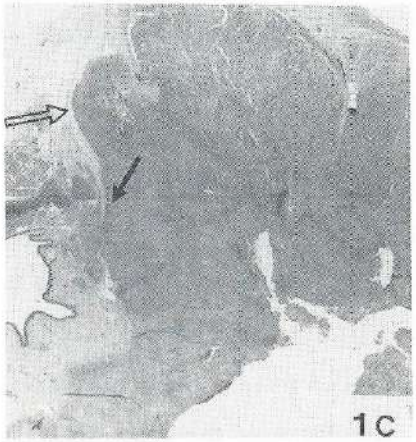
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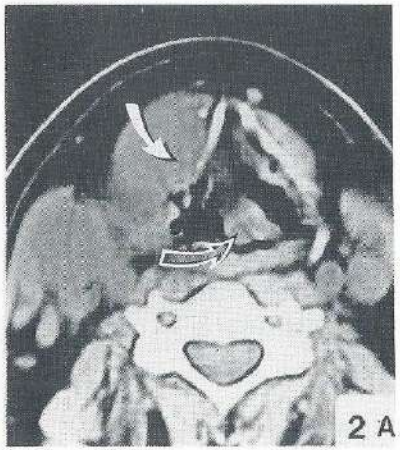
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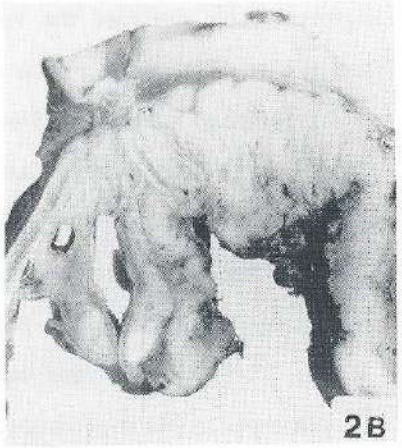
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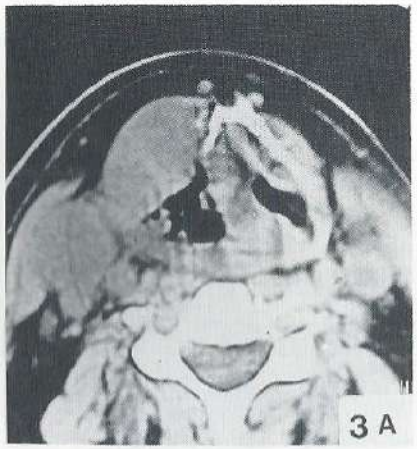
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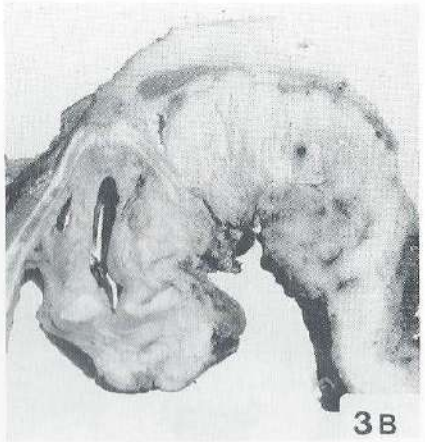
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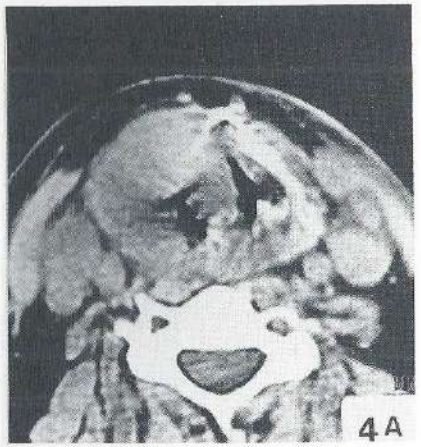
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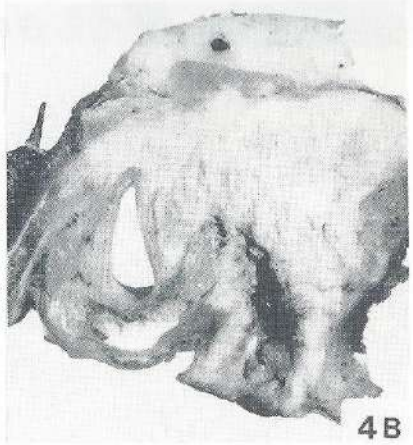
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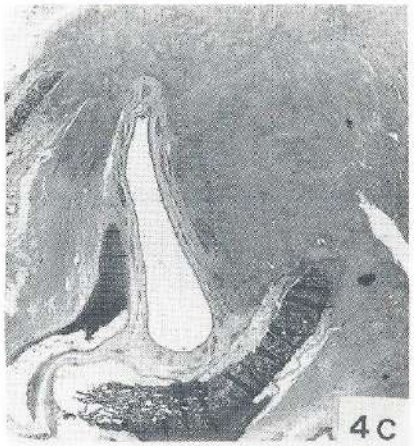
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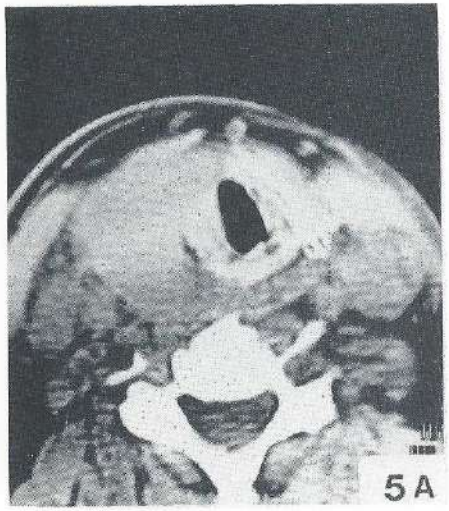

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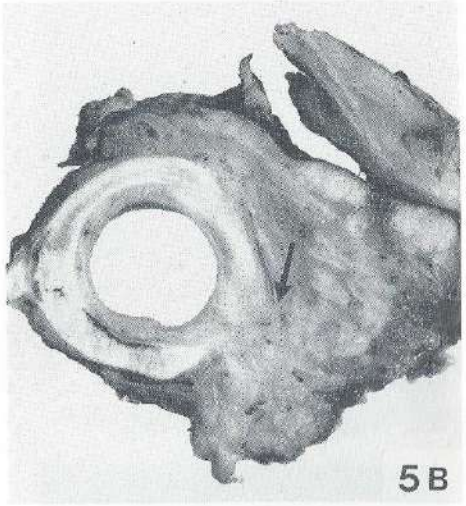

5B

5C

this finding. The tumor is very near to the cricoid ring and is probably invading the perichondrial lining of the cricoid (Fig. 5c).

Comment

This last demonstration is illustrative for the mode of laryngeal

invasion of a piriform sinus lesion. Such an advanced lesion is very likely to infiltrate into the PLS. In this case clinical examination did indicate this growth pattern. The CT scan confirmed this finding. In fact, the contours of such a process can also be delineated by conventional radiologic techniques. The value of CT scanning in this case lies primarily in its ability to visualise destruction of the thyroid cartilage and to delineate tumor invasion into the soft tissues of the neck.

The current discussion has focused on 7 illustrative cases. It can be recalled, however, that a total of 20 cases were investigated in the study. For the remaining 13 cases similar attention was paid to the capacity of CT to demonstrate tumor infiltration into the laryngeal compartments, cartilage destruction at the supraglottic, glottic and subglottic levels and to extralaryngeal tumor spread. The results are summarized below.

These additional 13 cases represent 2 supraglottic lesions, 10 glottic lesions and 1 piriform sinus lesion. As was the case in the 2 supraglottic lesions discussed previously, clear infiltration into the PES was seen on CT and confirmed histopathologically. One of the supraglottic lesions even showed clear cartilage destruction with extralaryngeal tumor spread. This was also confirmed histopathologically.

Of the 13 glottic lesions (the 3 previously described + the 10 additional cases) 9 were advanced lesions and 4 represented tumor recurrences after primary radiotherapy. Complete cartilage destruction was evident on CT in 2 cases, both of which were

confirmed histopathologically. Infiltration of the thyroid cartilage was suspect on CT in 5 cases, although such infiltration was demonstrated histopathologically in only 4. Conversely, 2 additional cases of infiltration were detected on histopathologic examination which were missed on CT scan. Thus, it can be concluded that CT diagnosed cartilage infiltration and destruction correctly in 6 out of 8 cases.

PLS involvement was seen in those cases where cartilage destruction was also present (6 cases). Involvement of the PLS was, however, found on histopathologic examination in all advanced lesions (9 cases). In those cases where extralaryngeal tumor spread was demonstrated by CT, it was also found after histopathologic examination. However, in 2 cases where CT only suspected tumor infiltration into the thyroid cartilage, extralaryngeal spread was also found histopathologically. There were no false positive results with regard to the extralaryngeal tumor spread.

The results of the CT-histopathologic examination of the piriform sinus lesion were comparable with those mentioned previously. That is, the CT indicated that the piriform sinus was replaced by tumor and that the thyroid cartilage was destructed. These findings were confirmed by histopathologic examination.

In the following discussion we will summarize, on the basis of our findings and those of other investigators, the value of CT for the assessment of the extension of laryngeal cancer.

Discussion

CT scan provides valuable additional information in the radiologic examination of laryngeal cancer. It represents, until now, the only radiologic method capable of visualising the extent of laryngeal carcinoma in the horizontal plane. This horizontal or axial plane offers a unique view of the laryngeal structures. Its application is therefore, particularly indicated in those cases where tumor infiltration into the horizontal plane is expected.

The results of our CT-histopathologic study, as described previously, are fundamentally in accordance with those of other investigators (74,75,76,77,78,79,80,81). The findings identify several areas in which CT can be of clinical value in the visualisation of the extent of laryngeal carcinoma. The pre-epiglottic space (PES), the thyroid cartilage and the extralaryngeal soft tissues which should be mentioned first. The paralaryngeal space (PLS), the anterior commissure and the subglottic larynx seem to be of minor importance but CT still gives a good deal of additional information about these structures.

The pre-epiglottic space (PES)

CT is of value in delineating tumor infiltration into the PES. Similar to the findings of previous investigators (51,82), case IV underscores the value of CT in the visualisation of such tumor infiltration. We found CT to give excellent visualisation of the PES. It was confirmed that the PES has both a characteristic

configuration and a characteristic tissue density on the scan. Therefore, the PES is more accurately defined by CT scan than by any other radiologic or clinical modality. Compared to CT it seems that the various radiologic methods demonstrate only gross invasion. CT scan differentiates between soft tissues of similar density, thus providing more precise information about tumor involvement. We consider CT to be an indispensable adjunct in the diagnostics of tumor infiltration into the PES.

The thyroid cartilage

The ability of CT to visualise cartilagenous structures in the horizontal plane represents another important advance in the radiologic assessment of tumor extension (88,89,90). Our results indicate that CT is valuable in demonstrating cartilage destruction, particularly in cases where a large tumor mass is present. These findings are confirmed in literature (90,91,92,93,94,95,96).

CT can also detect invasion of smaller lesions but only when the thyroid cartilage is not calcified. When the thyroid cartilage is partly calcified the tumor can not always be differentiated from the adjacent calcified tissue, due to the fact that the tumor and the calcified portion of the cartilage can be of equal tissue density on the scan. These findings confirm those of Parsons et al (94).

On CT scan the cortical layers of the thyroid cartilage can not be identified as distinct structures. Nevertheless, we can conclude that CT proves to be a much more sensitive method than either

clinical or conventional radiologic examination where even complete destruction of the thyroid cartilage may go undetected.

The extralaryngeal soft tissues

Most tumors with extralaryngeal soft tissue involvement are not readily palpable. Only some of the severe anterior tumorous extensions can be detected by clinical examination. According to previous findings of other investigators (51), the diagnostics of tumor spread outside the larynx is facilitated by CT. Anterior to the laryngeal skeleton the infra-hyoid strap muscles are well recognised on the scan. Tumor infiltration into these structures is readily visualised by CT. In some cases even asymmetry of the contour of the neck can be seen under these circumstances.

Conventional radiologic examination does not give much additional information about the extension of extralaryngeal tumor growth. Therefore, we can conclude that it is the CT scan that helps us to confirm this tumor spread by its unique horizontal view. As a consequence, staging of tumors infiltrating the extralaryngeal soft tissues becomes far more exact prior to treatment.

The paralaryngeal space, the anterior commissure region and the subglottic larynx

While CT provides more detailed diagnostic information about the PES than do conventional radiologic procedures, i.e. frontal tomography and laryngography, it does not increase significantly our ability to

delineate tumor infiltration into the PLS. In fact, CT fails to delineate the laryngeal ventricle, while it is clearly demonstrated by frontal tomography. Only in case of tumor infiltration into the PLS with possible destruction of the thyroid cartilage is CT of more value than the conventional radiologic methods.

Conventional tomography provides insufficient information about the extent of a laryngeal carcinoma into the anterior commissure region. CT improves the diagnostics of tumor infiltration in this area. The configuration of the anterior commissure region on CT scan is characteristic and has been described earlier. Prior investigators have also examined extensively the configuration and visualisation of the anterior commissure region by CT (83,84,85). Any tissue thickening of the intramucosal lining in the anterior commissure region should be regarded as pathologic. Tissue thickening of the intramucosal lining has been clearly demonstrated previously. This pathologic finding appears to be a most important contribution of CT to the diagnostics of the anterior commissure region.

Subglottic extension can easily be assessed by direct laryngoscopy and frontal tomography. In chapter II we mentioned the conus elasticus and the crico-thyroid membrane as important structures in defining the spread of a subglottic tumor. Invasion of the conus elasticus is well demonstrated by CT and possible destruction of this structure can be detected in an early stage. It is generally agreed that in case of destruction of the conus elasticus infiltration of the cricoid cartilage may occur. The value of CT lies in its ability to visualise this infiltration. In addition CT provides information about possible destruction of the crico-thyroid membrane and extra-laryngeal tumor growth.

Conclusion

Numerous recent improvements and technical advancements make CT a feasible diagnostic technique for studying laryngeal carcinoma. New technology has shortened the period of performing CT procedures and has improved spatial resolution considerably. The radiation dose has been reduced to about 50% of the radiation dose of conventional X-ray techniques.

Beyond these technical improvements the fundamental value of CT in the diagnostics of laryngeal cancer is found in its ability to visualise tumor extension in a horizontal plane. CT is therefore of great importance for the visualisation of tumor infiltration into the PES, the thyroid cartilage and the extralaryngeal soft tissues. The use of CT in the visualisation of the PLS, the anterior commissure region and the subglottic larynx were also discussed but its value in these areas appears to be of lesser importance.

CHAPTER V

CT AND THE MANAGEMENT OF LARYNGEAL CANCER

In this chapter the significance of CT for the primary treatment of laryngeal cancer will be discussed in relation to the various T-stages of the tumors as classified by the TNM system of the UICC.(6). This will be done on the basis of our own findings with CT in laryngeal cancer, as discussed in the previous chapter, and of those reported in literature.

CT and the management of T_1 laryngeal cancer

T_1 glottic carcinoma.

The T_1 glottic tumor represents a lesion confined to the glottic region with normal vocal cord mobility. If the tumor is limited to one vocal cord the lesion is classified as T_{1a}. If the tumor involves both vocal cords the lesion is registered as T_{1b} (6). High cure rates are obtained with either radiation therapy or surgical resection.Successful surgical techniques include, among others, hemi- or frontolateral laryngectomy and CO_2 laser surgery (7,9,99,105).

Since local control of the lesion is equally satisfactory with either modality of treatment, the method of choice depends mainly on the functional results obtained (9). Radiotherapy is, therefore,

generally preferred, with surgery in reserve for radiation failures (7,106,108,109).

It is generally agreed that CT does not provide much additional information about the extent of the T_1 glottic lesion as assessed by routine clinical and conventional radiologic examination (51). Frontal tomography and laryngography are of more value in delineating precisely small intralaryngeal irregularities.

T_1 supraglottic carcinoma

The T_1 supraglottic tumor represents a lesion confined to its region. The tumor can be limited to the laryngeal surface of the epiglottis or to an ary-epiglottic fold, a ventricular band or ventricular cavity. Under these conditions the lesion is registered as T_{1a}. If the tumor of the laryngeal surface of the epiglottis extends unilaterally or bilaterally to the ventricular band or cavity, it is classified as T_{1b}. Normal mobility of the vocal cords is a prerequisite for both registrations (6).

Early supraglottic lesions are successfully treated by conservation surgery. Conservation surgery provides excellent functional results and satisfactory survival rates (101,102,103). According to the findings of Olofsson et al (29) the results of supraglottic laryngectomy are superior to those after primary radiotherapy.

Several fundamental rules should be taken into account when considering a supraglottic laryngectomy (27,103). They primarily concern the extent of the lesion. One of the criteria is that there must be a 5 mm margin between the lower margin of the tumor and

the anterior commissure. Further, the vocal cords should be mobile and the thyroid cartilage should be free of disease. CT assists in determining the extent of the thyroid cartilage destruction. It is, therefore, clear that CT findings provide information valuable in deciding whether or not a supraglottic laryngectomy is indicated.

Most of the smaller supraglottic lesions are confined to the epiglottis. If a supraglottic lesion spreads bilaterally or in depth, deep invasion into the PES is not uncommon. It has also been demonstrated that CT is capable of visualising this extension. Visualisation of tumor infiltration into the PES does not contra-indicate a supraglottic laryngectomy. One should, however, be aware of such extension during operation. Visualisation of superior tumor extension into the valleculae or base of tongue is also important. If tumor extension into these structures is present and if a supra-glottic laryngectomy is under consideration, the extension as seen on the scan should be taken into account seriously to delineate the superior margin of resection precisely.

If conservation surgery is not under consideration anymore, due to either the extension of the lesion or to a less vital pulmonary function in combination with a poor general condition of the patient, radiotherapy is the treatment of choice.

From the foregoing we may conclude that, although CT appears to be of minor value in the management of T_1 glottic lesions, it can have its influence on the choice of treatment of T_1 supraglottic tumors.

T_1 subglottic carcinoma

T_1 sublottic lesions can be divided in T_{1a} and T_{1b} lesions. The T_{1a} lesion is found on one side of the subglottic region. The T_{1b} tumor extends to both sides (6). Radiotherapy is preferable in both cases. However, when infiltration of the cricoid cartilages or destruction of the crico-thyroid membrane is present, the results of radiotherapy seem to be less favorable (105). CT informs us about the infiltration into the cricoid cartilage or into the lower margin of the thyroid cartilage. The influence of CT on the choice between radiotherapy or surgery is of more relevance in case of a T_2 subglottic lesion.

CT and the management of T_2 laryngeal cancer

A T_2 lesion represents a tumor confined to the larynx, and to the region of origin with extension to an adjacent region. That is, a T_2 supraglottic lesion is a lesion of the supraglottic region with extension to the glottic level (6). A T_2 glottic lesion extends to either the supraglottic or subglottic region or to both regions. A T_2 subglottic lesion extends to the glottic level. In all cases total fixation should be absent. Impaired mobility of the vocal cords, however, is included in the classification of the T_2 lesions (6). In general, radiotherapy is the method of choice in the treatment of T_2 laryngeal lesions. The surgical alternatives are less attractive, in that a total laryngectomy is almost always required.

The response of laryngeal cancer to radiotherapy is directly related to several general factors including the patient's physical condition

and sex. The average overall control probability for laryngeal cancer by radiotherapy in females appears to be around 70%, compared to less than 50% in males (8,98,106,107). Furthermore, the presence of general disease such as diabetes, chronic cardiovascular and pulmonary failures are risk bearing factors in radiotherapy (9,107).

Other more specific factors influencing the response to radiotherapy are the histology of the tumor, the site of origin of the carcinoma, the extent of the lesion and the nature of tissues involved. With regard to the latter factor, elastic structures including the epiglottis and conus elasticus as well as muscular structures, such as the thyro-arytenoid muscle are less sensitive to radiotherapy (8). In particular, tumor infiltration into cartilagenous structures reduces the radiation response. Radiotherapy is incapable of sterilising the malignant cells invading the hyalin cartilages. If these supportive structures are infiltrated by tumor, radiation often results in perichondritis, necrosis or sequestration of the cartilages, particularly if high doses of radiation are given. It is known that the risk of complications in radiotherapy rises once the dose of 2050 NSD has been exceeded (110). Therefore, surgical intervention should be taken into account in case of cartilage infiltration.

Considering the UICC classification, T_2 tumors represent a rather heterogeneous group. The nature of tissues involved varies greatly. Within the definition of T_2 tumors significant differences in volume and extent may be present. A T_2 glottic lesion may, for example, be a small tumor, but may also represent a large transglottic lesion with impaired mobility of the vocal cord.

Local control rates by radiotherapy reported in literature vary from 40 to 80% (98, 111). Harwood (112) compared local control rates, with radiotherapy, in T_2 glottic lesions with normal vocal cord mobility as opposed to T_2 glottic tumors with impaired vocal cord mobility. Where normal vocal cord mobility was present, the lesion was controlled locally by radiotherapy in approximately 76% of cases. In contrast, only approximately 51% of cases with impaired mobility were controlled by radiotherapy. No differences in local control rates were found in those cases where increasing degrees of only superficial tumor extension were present. Thus, in the infiltrative type of tumor growth did the local control rate decrease.

These findings indicate that increased tumor infiltration influences the prognosis significantly. Precise delineation adds a good deal of information about the risk of failures and possible complications of radiotherapy. CT is capable of detection of the variations in volume, infiltration and extent of the T_2 lesion. Therefore, CT will identify those cases in which these complications and failures can be expected.

CT and the management of T_3 and T_4 laryngeal cancer

According to the UICC criteria, a T_3 laryngeal lesion represents a tumor confined to the larynx with fixation of one or both vocal cords or other evidence of deep infiltration. A tumor is classified as T_4 when it demonstrates extralaryngeal tumor growth (6). After histopathologic examination, however, it is not uncommon to find that large T_3 lesions do extend beyond the confines of the laryngeal

framework. T_4 lesions, on the other hand, do not always demonstrate vocal cord fixation. Therefore we do not consider the distinction between T_3 and T_4 lesions to be as strict as suggested by the UICC classification rules. We consider the term "advanced tumors" to be more comprehensive for the larger T_3 and T_4 laryngeal lesions. The inability of the clinician to determine the extent of malignant growth within the deep planes of the larynx represents serious limitations in the management of the advanced lesions. In his thesis "Surgical treatment of laryngeal cancer in the Netherlands" de Jong discussed the reliability of preoperative clinical examination (113). He found that the reliability was lowest when the tumor extended outside the laryngeal skeleton. Extralaryngeal growth patterns were detected clinically in only 32% of cases. Similarly, Olofsson, in his study on serial sectioning of the larynx, argued that the extension of the advanced lesions was underestimated in more than 50% of cases (19).

Conventionally, advanced tumors are treated primarily by surgery due to the fact that the results of total laryngectomy are better than those of primary radiotherapy (7). Surgical treatment can be combined with pre- or postoperative radiotherapy. More recently, some authors have advocated primary radiotherapy with surgery in reserve for the advanced case. They argue the small gain in 5 year survival rate not to justify the increased number of laryngectomies (9,98,105). This more conservative approach has an appeal. However, it seems to be worthwhile to mention certain limitations in this approach. Firstly,it is known that the response of the larynx to radical doses of radiotherapy varies from mild erythema to severe

edema and induration. Although radionecrosis is uncommon with the modern radiotherapeutic techniques, it is still reported in recent literature to occur, particularly in the advanced supraglottic laryngeal lesion, where tumor infiltration into the laryngeal cartilages or extralaryngeal tumor growth is present (114). Intralaryngeal edema is more common. Severe edema makes adequate control by mirror examination extremely difficult. Residual disease or tumor recurrence can be missed easily. Radiotherapy furthermore increases the surgical complication rate of salvage surgery, when this has to be carried out for a recurrent disease. It is clear that these considerations indicate the need for a more circumscript selection of patients before primary treatment.

CT helps to select those patients in which the chances of cure by radiotherapy are reduced due to cartilage invasion or due to a large tumor volume, with or without extralaryngeal tumor growth Such cases would remain undetected using only clinical and conventional radiologic methods. CT, therefore, has an influence on the treatment policy of the advanced laryngeal tumor, providing information necessary to choose between radiotherapy and surgery.

SUMMARY

Cartilage invasion and extralaryngeal tumor growth, as a result of deep tumor infiltration of the advanced laryngeal carcinoma, is often underestimated by clinical and conventional radiologic examination. Such a growth pattern influences the treatment policy of laryngeal cancer. Therefore, it is generally agreed that there is a need for a more accurate assessment of the extent of the advanced laryngeal carcinoma. Compared to clinical and conventional radiologic examination, CT has the unique capacity to visualise tumor extension in the transverse plane. It, therefore, provides information valuable in the assessment of extension of laryngeal cancer. This thesis discusses the role of CT in the management of laryngeal cancer.

In chapter I the anatomy of the normal larynx is described. Particular attention is paid to the configuration of the laryngeal cartilages and the laryngeal compartments. The cartilages are considered as unmistakable landmarks for the understanding of the anatomy, as seen on the scan.

In chapter II the patterns of growth and spread of laryngeal cancer are described. The anatomical division of the larynx into a supra-glottic, glottic and subglottic region can be used for a precise description of the extent of the primary lesion. The modes of tumor spread are discussed. The laryngeal compartments are mentioned as important areas of possible tumor infiltration. Special attention is paid to the infiltrative growth of lesions in the anterior commissure region and the pattern of tumor spread into the thyroid cartilage is described.

In chapter III the clinical examination and conventional radiologic examination of laryngeal cancer are discussed. Indirect laryngoscopy gives a good overall survey of the intralaryngeal structures. Nevertheless, certain recesses of the larynx are inaccessible for mirror examination alone. Direct laryngoscopy and fiberoptic laryngoscopy are an indispensable completion to mirror examination. In this chapter the techniques of the conventional radiologic examination are described as well. Particular attention is paid to conventional frontal tomography. Although this technique has its shortcomings, it provides reliable visualisation of the extent of the intralaryngeal tumor.

In chapter IV the principles of CT examination and the role of CT scan in the visualisation of the extension of laryngeal carcinoma are discussed. CT images of the normal and pathologic larynx are demonstrated. Brief attention is paid to scan views of soft tissue structures in the neck. Furthermore, a comparative CT-histopathologic study is described. Seven illustrative cases, in which the CT examination is compared with the histopathologic examination of the excised larynges, are presented. CT is of particular value in the visualisation of tumor invasion into the pre-epiglottic space, the thyroid cartilage and the extralaryngeal soft tissues.

In chapter V the significance of CT for the primary treatment of laryngeal cancer is discussed in relation to the various T-stages of the tumors as classified by the TNM system of the UICC. CT scan is of little value in T_1 tumors. On the contrary, CT scan helps to select those patients with advanced laryngeal carcinoma in which the

chances of cure by radiotherapy are reduced due to cartilage invasion, a large tumor volume or extralaryngeal tumor growth. Therefore, CT has its influence on the treatment policy of, particularly the advanced laryngeal carcinoma.

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Het klinisch, endoscopisch en conventioneel röntgenologisch onderzoek laten een nauwkeurige bepaling van de plaatselijke uitbreiding van zich in een gevorderd stadium bevindende larynxcarcinomen niet toe. Dit geldt vooral voor aantasting door de tumor van het kraakbeenskelet van de larynx en voor extralaryngeale tumoruitbreiding. In tegenstelling tot de genoemde onderzoekmethoden biedt het computer tomografisch onderzoek de unieke mogelijkheid de uitbreiding van de tumor in het horizontale vlak te bepalen en daarmee in het bijzonder informatie te verschaffen over eventuele aantasting van het kraakbeenskelet en extralaryngeale tumorgroei. In dit proefschrift wordt de waarde van het computer tomografisch onderzoek voor de diagnostiek en de behandeling van het larynxcarcinoom besproken.

In Hoofdstuk I wordt de anatomie van de larynx beschreven. Speciale aandacht wordt besteed aan de configuratie van het larynxskelet en de zogenaamde laryngeale compartimenten.

In Hoofdstuk II wordt de groeiwijze van het larynxcarcinoom besproken. Daarbij wordt de gebruikelijke indeling in supraglottische, glottische en subglottische carcinomen gevolgd. De wijze waarop de tumor zich binnen de laryngeale compartimenten kan uitbreiden, wordt besproken. In het bijzonder wordt aandacht besteed aan de wijze waarop larynxcarcinomen het kraakbeenskelet kunnen aantasten en zich tot buiten het larynxskelet kunnen uitbreiden.

In Hoofdstuk III wordt het klinisch en conventioneel röntgenologisch onderzoek van het larynxcarcinoom besproken. De indirecte laryngoscopie geeft een goed overzicht van de intralaryngeale structuren. Bepaalde delen van de larynx zijn echter niet toegankelijk voor de indirecte laryngoscopie. De directe en de flexibele laryngoscopie vormen een aanvulling op het spiegelonderzoek. In dit hoofdstuk worden tevens de technieken van het conventioneel röntgenologisch onderzoek beschreven. Speciale aandacht wordt besteed aan de voor-achterwaartse tomografie. Hoewel deze techniek zijn beperkingen kent, geeft zij vooral een betrouwbare afbeelding van de intralaryngeale tumoruitbreiding.

In Hoofdstuk IV worden de principes van de computer tomografie en de waarde van het computer tomografisch onderzoek voor de visualisatie van de tumoruitbreiding van het larynxcarcinoom besproken. Computer tomografische beelden van de normale en pathologische larynx worden vertoond. Tevens wordt in het kort aandacht besteed aan scan-beelden van de weke delen in de hals. Voorts wordt een vergelijkende studie betreffende computer tomografisch en histopathologisch onderzoek van het larynxcarcinoom beschreven. Er worden zeven illustratieve gevallen besproken, waarin de bevindingen van preoperatief uitgevoerd computer tomografisch onderzoek van de larynx worden vergeleken met postoperatief verricht histopathologisch onderzoek van het verwijderde larynxcarcinoom. Uit dit onderzoek blijkt dat het computer tomografisch onderzoek met name waardevol is voor de visualisatie van tumoringroei in de pre-epiglottische ruimte, in het larynxskelet en in de aangrenzend extralaryngeale weke delen van de hals.

In Hoofdstuk V wordt het belang van het computer tomografisch onderzoek voor de primaire behandeling van het larynxcarcinoom besproken in relatie tot het T-stadium van de tumor, overeenkomstig de TNM classificatie van de UICC. De waarde van het computer tomografisch onderzoek bij T_1 larynxtumoren lijkt gering. Het computer tomografisch onderzoek is evenwel van groot belang voor het selecteren van die patienten met een larynxcarcinoom bij wie de kans op genezing met behulp van radiotherapie verminderd is als gevolg van tumoringroei in het larynxskelet, een groot tumor-volume of extralaryngeale tumoruitbreiding. Het computer tomografisch onderzoek kan dan ook in het bijzonder een bijdrage leveren tot de keuze van behandeling van patienten met een larynxcarcinoom in een gevorderd stadium.

STELLINGEN

1. Bij patienten met een plaveiselcelcarcinoom van de larynx dient computer tomografie van de larynx als een verplicht onderdeel van de diagnostiek beschouwd te worden met het oog op adequate stagiering in het kader van de TNM classificatie.

2. Computer tomografisch onderzoek van de larynx maakt conventionele voor-achterwaartse planigrafie van de larynx overbodig bij patienten met een larynxcarcinoom.

3. Ondanks de hooggekoesterde verwachtingen ten aanzien van diagnostisch onderzoek met behulp van de NMR (Nuclear Magnetic Resonance), zal de computer tomografie de superieure onderzoeksmethode blijven voor de diagnostiek van het larynxcarcinoom.

4. De primaire behandeling van patienten met een plaveiselcelcarcinoom van de tong groter dan 2 cm in de grootste diameter, dient chirurgisch te zijn.

5. Indien palliatieve chemotherapie wordt overwogen bij patienten met een plaveiselcelcarcinoom in het hoofd-halsgebied, verdient zogenaamde monochemotherapie met methotrexaat nog steeds de voorkeur boven zogenaamde polychemotherapie.

6. Indien tot een gecombineerde behandeling met chirurgie en radiotherapie bij patienten met een plaveiselcelcarcinoom in het hoofd-halsgebied wordt besloten, dient de chirurgische behandeling vooraf te gaan aan de radiotherapeutische.

7. Electieve behandeling van de hals van een patient met een carcinoom in de mondholte of orofarynx dient chirurgisch te zijn.

8. Bij verdenking op een cholesteatoom verdient de planigrafie volgens Guillen de voorkeur boven andere conventioneel röntgenologische onderzoeksmethoden.

9. Immuunhistochemische bepaling van het plasmacel patroon in dikke darm biopsieën is een belangrijk hulpmiddel voor de differentiaal-diagnostiek van acute infectieuze colitis, M. Crohn en colitis ulcerosa.

10. In de behandeling van stadium I en II Non-Hodgkin lymfomen met een hoge maligniteitsgraad van de bovenste lucht- en voedselweg verdient chemotherapie een vaste plaats.

11. De kosten gemaakt voor kinderoppas dienen in elk gezin met tweeverdieners belasting aftrekbaar te worden gesteld als kosten van verwerving. Anders worden ongewenste werkloosheid, kinderloosheid en belastingfraude bevorderd.