Glottic Cancer of the Free Margin and Ventricular Surface of Vocal Cord

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The authors differentiate cancer types of the glottis setting out from the free margin or the ventricular surface of the true vocal cord. The latter is considered to be a reliable clinicopathological unit starting from the dividing line of the stratified-ciliated epithelium margins, whereas the so called junctional tumor differs in its histogenesis and invasivity. They give a detailed description of intralaryngeal extension of these tumours on the basis of histopathological investigations. (Pathology Oncology Research Vol 2, No1–2, 43–47, 1996)

Key words: glottic cancer, intralaryngeal spread, histopathology

Introduction

A considerable amount of data is available on mechanisms involved in the spread of laryngeal cancer. However, our knowledge is not complete so further investigation is necessary. Vocal cord tumors grow within the margins of the glottic region for a period of time. The progression of these cancers is lower than that of supraglottic tumors. The course might also be different among various types of glottic malignancies of the same size. We carried out the following studies in order to find a morphological explanation of this phenomenon.

Materials and methods

During the past six years more than 150 patients were treated for vocal cord cancer in our departments and 83 of them were treated surgically. Light and electronmicroscopic investigations were carried out on laryngectomy specimens. Tumor samples were histologically-proven to be either keratinizing or non-keratinizing squamous cell carcinoma. For light microscopy, so-called whole organ serial sections were cut, and hematoxylin-eosin, Mallory and Goldner trichrome stainings were performed. For electronmicroscopic investigations, tumor specimens were placed in 2.5 % glutaraldehyde fixative buffered to pH 7.4 with sodium cacodylate, while 2 % osO, was used as a post-fixative. After dehydration, the material was embedded into Durcupan ACM (Fluka, Basle, Switzerland). The sections were contrasted with uranyl acetate and lead-citrate, and photomicrographs were taken with a Jeol JEM-100B electron microscope at an accelerating voltage of 60 kV.

Results

We divided vocal cord cancers into two groups: originated at the free margin or from the ventricular surface of the vocal cord (Fig.1).

Vocal cord tumors of the free margin

Endolaryngeal microscopy showed that the tumor initially grew out from the non-keratinising epithelium of the vocal cord. It may reach the anterior commissure, may grow to the opposite side or posteriorly, and may invade the processus vocalis. When the ventricular surface of the vocal cords is free from tumor, the ciliated epithelium can be well-distinguished by its rather livid color. By using whole organ slide series, it can easily be determined that tumors reaching the anterior commissure and processus vocalis do not infiltrate the paraglottic space (Fig.2). The
connective tissue surrounding the tumor is compact, fibrous and the behaviour of the tumor is less infiltrating. The widened connective tissue fibers form a cord-like barrier towards the paraglottic space. As determined by light microscopy there is peritumoral connective tissue full of lymphocytes and histiocytes around the groups of atypical and polymorph tumor cells (Fig. 3).

Figure 3. Border of the free margin vocal cord cancer mass and surrounding connective tissue. The peritumoral connective tissue is full of histiocytes. The margin of the tumor is sharp. (HE, 250 x)

With electron microscopic analysis, intact basal membrane can be seen between the tumor and surrounding connective tissue. The connective tissue contains mainly collagen fiber bundles, however hypertrophic fibroblasts are also present with a number of mitochondria, endoplasmic reticulum with cystern-like holes in their cytoplasms (Fig. 4).

For more advanced vocal cord tumor originating from the free margin, subglottic invasion is characteristic (Fig. 5). It

Figure 4. Border of the free margin vocal cord cancer mass and surrounding connective tissue. The basal membrane can be well-distinguished around the tumor cells. The connective tissue contains lots of collagen fibres. (Gomori argentiferric - lead citrate stain, 4000 x)
partly columnar epithelia and the tumor tissue containing polymorphic cells was detected at the junction of the two types of epithelia. Under electron microscope, the border of the tumor and the connective tissue is irregular and the tumor cells outlined by basal lamina deeply infiltrate the connective tissue. A smaller group of tumor cells breaking through the basal lamina was also seen. New basal lamina formation was not detected around these cells. In the connective tissue, the collagen fiber bundles showed a unique pattern in horizontal and vertical planes (Fig.9). In more advanced stages, the tumor even broke through the thyroid cartilage (Fig.10) and infiltrated the inferior region of the supraglottic area (Fig.11). The supraglottic spread of the tumor was indicated by the bypassing of the Morgagni-sack and infiltrating the false vocal cord by these cells. The expansion of the tumor downwards is limited by the conus elasticus, which forms a thick connective tissue barrier and drives the tumor between the inferior edge of the thyroid and the cricoid cartilage.

Discussion

Data on the spread, malignancy and prognosis of laryngeal cancer have pathological and clinical importance. There are several histopathological classification systems avail-

Vocal cord tumors of junctional origin

Among the glottic cancer patients, 18 tumors originating from the junctional zone of vocal cord, were treated surgically. By indirect laryngoscopy, junctional vocal cord tumors are seen next to the free edge of the vocal cords. In these cases, however, the tumor originates from the junction of stratified epithelium and columnar epithelium. When displacing the false vocal cords during endolaryngeal microscopy, the progression of the tumor can be detected towards the Morgagni-sack. We determined by using whole-organ slide sections that the junctional vocal cord tumor even in early stages infiltrates the paraglottic space and can expand as far as the thyroid cartilage (Fig.7). Upwards does not involve the false vocal cord. The barrier for subglottic expansion of the tumor is the conus elasticus. In contrast the paraglottic space containing loose fibrous connective tissue enables tumor progression, which was detected by microscopic studies showing the infiltrating behaviour of the carcinoma (Fig.8). Histological analysis of the junctional vocal cord revealed that the tissue is covered by partly stratified.

Figure 5. Parasagittal whole organ section in the first third of the true vocal cord. Free margin type cancer in advanced stage the upper part of the paraglottic space and the Morgagni-sack is uninvolved. The tumor shows subglottic spread, and breaks through the conus elasticus. (CT = thyroid cartilage, E = epiglottis, M = Morgagni-sack, T = tumor). (Mallory stain)

Figure 6. Parasagittal whole organ section in the middle third of the true vocal cord. There are compact bundles of connective tissue in the Morgagni-sack around the tumor. The cancer spreads subglottically over the upper part of cricoid cartilage. The supraglottic region and the upper part of the paraglottic space is free from tumor. (CT = thyroid cartilage, E = epiglottis, T = tumor). (Mallory stain)
been drawn to the role of cartilaginous and connective tissue in the expansion of laryngeal cancer. On the basis of these data, the diagnostic and therapeutic importance of tumor invasion can be elucidated. However, most studies were performed in advanced cases. Although some aspects of the microinvasion of the tumor have been investigated, the direct clinical relevance of these data is not fully clear.

Figure 7. Parasagittal whole organ section. The paraglottic space is infiltrated by the junctional cancer. The tumor reaches the thyroarytenoid muscle. The lower bundles of the quadrangular membrane are uninvolved despite the supraglottic spread of tumor. The false vocal cord is free from tumor. Dyen, the conus elasticus forms a compact barrier of connective tissue. (Tr= functional tumor, CT= thyroarytenoid muscle, CE= conus elasticus). (Goldner trichrome)

Figure 8. The peritumoral part of a vocal cord cancer originated from the junctional zone by light microscopy. The infiltrative behaviour of the tumor cell groups can be seen on the photo. (HE, 250x)

Figure 9. Junctional vocal cord cancer by electron microscopy. The junction of the tumor and connective tissue is irregular. The smaller group of tumor cells is in the connective tissue and there is no basal lamina around them. There are also horizontal and vertical sections of collagen bundles. (Uranyl acetate and lead citrate)

Figure 10. Horizontal section of the larynx. This advanced stage cancer originating from the junctional zone infiltrates the paraglottic space. (CT= thyroarytenoid muscle, CA= arytenoid cartilage, Tr= tumor). (Goldner trichrome stain)
The term "transglottic" cancer has been defined based on the intralaryngeal spread of the carcinoma. However, this category also includes the supraglottic tumors spreading downwards, the glottic tumors growing upwards as well as malignancies originating from the Morgagni-sack.\(^\text{2,4}\)

In our study, we distinguished vocal cord cancer originating from the free margin or the junctional zone of the vocal cords. The major differences in histology rely on the malignant transformation of the stratified, non-keratinizing epithelium of the free margin versus that of the epithelial junction of the ventricular surface.

In the case of the free margin vocal cord cancer, the morphological explanation of the slower tumor progression is based on the compact connective tissue of the glottic region and the increased activity of histiocytes.

Our studies also point out the importance of the paraglottic space with loose connective tissue, which enables the spread of tumors of junctional origin. Thus, these tumors infiltrate the paraglottic space at very early stages. Preformed connective tissue structures determine the spread of the tumor: laterally the thyroarytenoid membrane, thyroid cartilage, superior and inferior tumor spread is limited by the quadrangular membrane and conus elasticus, respectively.

Though the vocal cord cancer originating from the free margin stays long within the glottic area, its subglottic spread is not limited by conus elasticus. The quicker progress of the junctional cancer infiltrating even the paraglottic space is considered to be due to the anatomically loose connective tissues of paraglottic space and to the poorer activity of connective tissue substances.

We think that the junctional vocal cord cancer ought to be distinguished from those originating from the free margin of the vocal cord. They are two different clinical entities, with differences in their histogenetic characteristics, as well as intralaryngeal spread. The frequency of the junctional vocal cord cancer cases was less than 20%. Among our patients non-identified junctional vocal cord cancers had previously been classified as glottic tumors or Morgagni-sack tumors. We suggest that our patho-anatomical and histological studies may have relevance for future, more advanced complex therapy of laryngeal cancer. Thus organ-conserving and reconstructive surgery could be even more effective.

References