

## Malignant sialogenic tumours of the larynx

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### Abstract

Laryngeal manifestations of malignant sialogenic neoplasias are rare. This paper documents the clinical features, treatment, biological behaviour and prognosis of 15 cases of malignant sialogenic tumours of the larynx that were reviewed in a retrospective clinical and histopathological study. The 15 cases of malignant sialogenic tumours of the larynx were diagnosed at the University Hospital, Eppendorf, over a period of 33 years (1965–1998). Forty per cent were adenoid cystic carcinomas, 33 per cent mucoepidermoid carcinomas and 27 per cent were poorly differentiated adenocarcinomas. Local tumour resection, if necessary in combination with bilateral neck dissection and post-operative radiotherapy, was associated with a five-year survival rate in 80 per cent of the mucoepidermoid carcinoma cases. Adenoid cystic carcinoma was associated with a less favourable five-year survival rate of 33 per cent. Low-differentiated adenocarcinomas were associated with the least favourable prognosis with a five-year survival rate (25 per cent). The prognosis for these tumours is thus poorer than for squamous cell carcinomas with the same localization and TNM status.

**Key words:** Laryngeal Neoplasms; Carcinoma, Adenoid Cystic; Carcinoma, Mucoepidermoid; Adenocarcinoma

### Introduction

The minor salivary glands are tubuloalveolar, mainly mucus-secreting glands ubiquitously found in the submucosa of the upper aerodigestive tract. They are mainly located in the oral cavity, particularly in the region of the hard palate, and to a far lesser degree in the nasal cavity, paranasal sinuses, pharynx and larynx. The physiological importance of these glands and their secretory products lies in protecting the epithelium and in supporting deglutition and taste sensation.

Whereas major salivary gland tumours are most frequently benign, 36–91 per cent of the minor salivary gland tumours are malignant.<sup>1–5</sup> When classified according to the histopathological WHO classification of salivary gland tumours, adenoid cystic (32–69 per cent) and mucoepidermoid carcinomas (15–35 per cent) are the most frequent malignancies of the minor salivary glands.<sup>1,2,4–7</sup> Carcinomas in pleomorphic adenomas, acinic cell carcinomas and polymorphic low-grade adenocarcinoma also occur but are less common.<sup>1,4,5,7</sup>

The aetiology of most tumours of the minor salivary glands is unclear. Chemical noxae such as exposure to asbestos or lead,<sup>3</sup> alcohol abuse,<sup>8</sup> viral factors,<sup>9</sup> ionizing rays,<sup>10</sup> and genetic risk factors<sup>11</sup> are generally discussed as causative factors for the development of salivary gland malignancies. Chronic

wood dust exposure is a definite predisposing factor for adenocarcinomas in the minor salivary glands of the nasal cavity and paranasal sinuses.<sup>12,13</sup>

Corresponding to the topographic frequency distribution of minor salivary glands, most malignant sialogenic tumours are located in the oral cavity and laryngeal manifestations of these tumours are rare.<sup>14–17</sup> Due to the rarity of laryngeal neoplasias and the different histological tumour types, therapeutic decisions have thus far been frequently made empirically from case to case.

In this study the localization and symptomatology and particularly the biological behaviour and prognosis of malignant sialogenic tumours of the larynx were examined in a retrospective clinical and histopathological study. In addition, prognosis was compared with that of laryngeal squamous cell carcinomas.

### Materials and methods

Malignant tumours of the minor salivary glands involving the larynx were diagnosed in 15 patients at the University Hospital, Eppendorf, between 1965 and 1998. Classification of the histopathological findings was done at the Hamburg salivary gland register. Patient-related data such as clinical findings, therapeutic procedures such as local tumour resection or laryngectomy (with/without neck dissection

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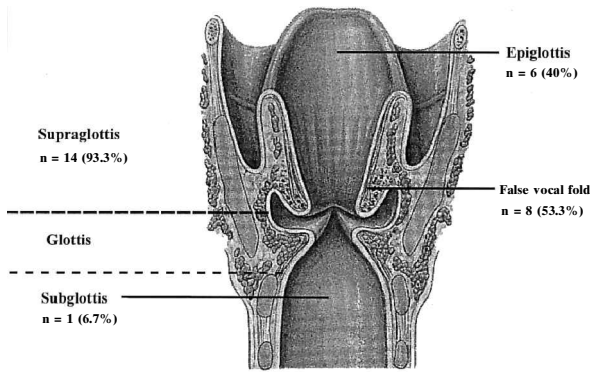


FIG. 1

Localization of the malignant sialogenic tumours of the larynx (n = 15).

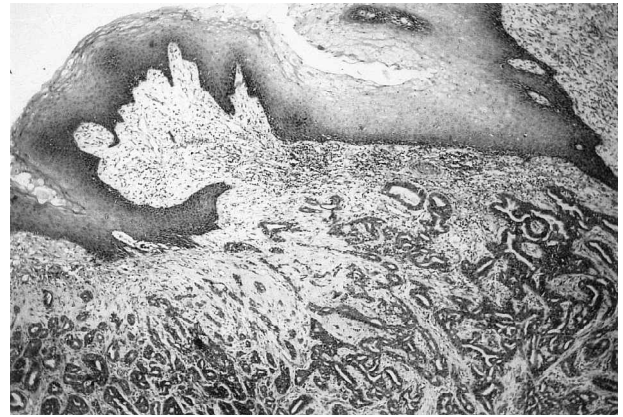


FIG. 2

Adenoid cystic carcinoma of the larynx (n = 6). (H & E;  $\times 16$ ).

and post-operative radiotherapy) and survival times, were researched on the basis of out-patient and in-patient records.

## Results

The median age of the 15 patients with malignant sialogenic tumours of the larynx was 56 years. The male/female sex ratio was 9:6.

The main clinical symptoms were dysphagia and hoarseness in 12 patients and respiratory problems in three patients. The duration of symptoms varied between three months and three years. Local findings were characterized by a submucosal mass under the intact mucosa in nine patients and by an exophytic tumour in six patients. In 14 cases, the tumour was localized in the supraglottis. In six of these patients the tumour was localized in the epiglottic region and in eight patients in the false vocal folds. In only one case was the tumour in the subglottis (Figure 1).

According to the histopathological WHO classification of salivary gland tumours and tumours of the upper respiratory tract,<sup>18</sup> six of the cases were adenoid cystic carcinomas (Figure 2). Of these three were of cribriform, and three were of solid tumours types. In five patients, the histopathological findings revealed a mucoepidermoid carcinoma: three of these tumours were classified as well differentiated (low-grade) and two as poorly differentiated

(high-grade) mucoepidermoid tumours. There were four cases with a poorly differentiated adenocarcinoma. Eight of 15 patients (53 per cent) had tumour stage pT<sub>3</sub> or pT<sub>4</sub>. Of these four had an adenoid cystic carcinoma and three a poorly differentiated adenocarcinoma (Table II).

Five out of the 15 patients had cervical metastases. These comprised one out of the six patients with adenoid cystic carcinoma, one out of the five patients with mucoepidermoid tumours and three out of four of the patients with adenocarcinoma.

All 15 patients underwent tumour resection. Laryngectomy was performed in 13 cases and supraglottic partial laryngeal resection in the remaining two cases. Ten patients also underwent bilateral neck dissection. The five patients with histopathologically detected cervical metastases underwent post-operative radiotherapy.

Six patients (40 per cent) developed a local recurrence. Two patients each with adenoid cystic carcinoma developed pulmonary metastases.

Five years after diagnosis, the following patients were considered tumour-free: one patient (25 per cent) with a poorly differentiated adenocarcinoma, two patients (33 per cent) with an adenoid cystic carcinoma and four patients (80 per cent) with a mucoepidermoid carcinoma. Thus, the mean overall five-year survival rate for all sialogenic laryngeal malignancies was 47 per cent.

TABLE I  
TNM STAGE, THERAPY AND FIVE-YEAR SURVIVAL OF THE MALIGNANT TUMOURS OF THE LARYNX

	Adenoid cystic carcinoma n = 6		Mucoepidermoid carcinoma n = 5		Adenocarcinoma n = 4	
TNM stage	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	n = 2	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	n = 1	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	n = 1
	T <sub>3</sub> N <sub>0</sub> M <sub>0</sub>	n = 3	T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	n = 1	T <sub>3</sub> N <sub>1</sub> M <sub>0</sub>	n = 1
	T <sub>3</sub> N <sub>1</sub> M <sub>0</sub>	n = 1	T <sub>2</sub> N <sub>1</sub> M <sub>0</sub>	n = 1	T <sub>3</sub> N <sub>2</sub> M <sub>0</sub>	n = 1
			T <sub>3</sub> N <sub>0</sub> M <sub>0</sub>	n = 1	T <sub>4</sub> N <sub>1</sub> M <sub>0</sub>	n = 1
Therapy	partial resection	n = 2	LE	n = 1	LE	n = 1
	LE	n = 1	LE + ND	n = 3	LE + ND + irradiation	n = 3
	LE + ND	n = 2	LE + ND + irradiation	n = 1		
	LE + ND + irradiation	n = 1				
5-year survival	2 (33.3%)	n = 1	4 (80%)		1 (25%)	

## Discussion

Malignant tumours of the minor salivary glands comprise less than one per cent of all laryngeal malignancies.<sup>19–21</sup> During a period of 33 years (1965–1998), 15 patients at the University Hospital, Eppendorf, were diagnosed as having a malignant sialogenic laryngeal tumour. The group size of 15 patients corresponds to that of previous reported series: three per cent (20 patients) of more than 600 patients with minor salivary gland tumours during a 30-year period,<sup>14</sup> 18 patients during a 38-year period,<sup>17</sup> 27 patients during a 35-year period.<sup>19</sup>

Sixty per cent of the malignant sialogenic laryngeal neoplasias in our study presented as a submucosal growth compared with a rate of over 80 per cent in other studies.<sup>16,17</sup>

In our series, 93 per cent of patients had a supraglottic tumour compared with 75 per cent in the series of Spiro *et al.* and Cohen *et al.*<sup>14,17</sup> This localization correlates with the topographic frequency distribution of minor laryngeal salivary glands which are found mainly in the region of the false vocal folds and the ventricles as well as below the anterior subglottic commissure.<sup>22</sup> The subglottic prevalence of 60–80 per cent<sup>16,23</sup> documented for adenoid cystic carcinomas was much higher than in our group (17 per cent).

In our study the patients' clinical picture correlated with the size and localization of the tumours in that the main symptoms were dysphagia and hoarseness. The pain symptoms reported for adenoid cystic carcinomas<sup>14,16,20</sup> were not observed in our study. In this study, symptoms had been for three weeks to three years<sup>16,23</sup> with a mean duration of 20 months.

In contrast to other studies,<sup>14,15</sup> the histopathological classification shows a predominance of adenoid cystic carcinomas (40 per cent) compared to mucoepidermoid carcinomas (33 per cent) and the poorly differentiated adenocarcinoma (27 per cent). In comparison, Spiro *et al.* reported 15 per cent as adenoid cystic carcinomas, 63 per cent as adenocarcinomas and 15 per cent as mucoepidermoid carcinomas.<sup>14</sup> Sessions *et al.* found adenoid cystic carcinomas in 33 per cent, adenocarcinoma in 45 per cent and mucoepidermoid carcinomas in 11 per cent of their cases.<sup>15</sup>

An advanced tumour stage (T<sub>3</sub> or T<sub>4</sub>) was documented in eight of our 15 cases (54 per cent) at diagnosis. Cohen *et al.*<sup>17</sup> reported advanced tumour stages in 12 of 18 (67 per cent) patients. This is in agreement with the review conducted by Spiro *et al.*<sup>14</sup> and Sessions *et al.*<sup>15</sup> Cervical metastases were observed in 17 per cent of our patients with an adenoid cystic carcinoma and in 75 per cent of our patients with an adenocarcinoma which corresponds to previous studies in which cervical lymph node metastases were found in less than 20 per cent of the patients with adenoid cystic carcinoma<sup>16,24</sup> and 68 per cent of patients with adenocarcinoma.<sup>19</sup>

The reported therapeutic procedures for sialogenic laryngeal tumours vary from therapeutic nihilism and radical surgery with pre- and post-

operative radio- and chemotherapy.<sup>14,21,25</sup> In our study, all 15 patients underwent tumour resection, either partial laryngeal resection or laryngectomy in accordance with the current primary surgical treatment concept.<sup>17,21,26,27</sup> Patients with a mucoepidermoid carcinoma or adenocarcinoma also underwent bilateral neck dissection. In contrast, amongst the patients with adenoid cystic carcinoma reviewed by Ferlito *et al.*<sup>24</sup> with adenoid cystic carcinoma neck dissection was only performed if there were clinically abnormal cervical lymph nodes and/or histologically confirmed cervical metastases. In our series, post-operative radiotherapy (per cutaneous irradiation) was applied in the five patients with an advanced tumour stage and histopathologically confirmed cervical metastases. Radiotherapy alone is purely palliative.<sup>17,19</sup> Patients with advanced poorly differentiated and already metastasizing tumours or adenoid cystic carcinomas should undergo post-operative or, if necessary, primary neutron beam radiotherapy, which promises to yield improved treatment results according to hitherto unpublished findings.

The prognosis of malignant sialogenic laryngeal tumours is co-determined by the histological tumour type and the differentiation grade. Whereas well differentiated (low-grade) mucoepidermoid carcinomas have a very favourable prognosis (five-year survival rate >95 per cent), poorly differentiated (high-grade) mucoepidermoid carcinomas have a much less favourable course (five-year survival rate <30 per cent).<sup>28,29</sup> In our study mucoepidermoid carcinomas had a prognostically favourable five-year survival rate of 80 per cent which correlated with the histological differentiation grade in that three were well differentiated (low-grade) and two were poorly differentiated (high-grade) mucoepidermoid tumours. Adenoid cystic carcinomas (three cribriform and three solid tumour type) were characterized by a high local recurrence rate and late distant metastases and had a much poorer five-year survival rate of 33 per cent. Comparable results (five-year survival rate of 31 per cent) were reported by Spiro *et al.*<sup>14</sup> The prognosis was least favourable for poorly differentiated adenocarcinomas with a five-year survival of 25 per cent. Cohen *et al.* reported a five-year survival of 42 per cent for adenocarcinomas.<sup>17</sup>

In accordance with the literature,<sup>14,17</sup> malignant sialogenic tumours – in this study mainly (93 per cent) supraglottic tumours – have a mean overall five-year survival rate of 47 per cent which is a poorer prognosis than squamous cell carcinomas of the same localization and tumour stage. For instance, Steiner documented an overall five-year survival of 59 per cent for patients undergoing transoral laser surgery for squamous cell carcinoma between 1979 and 1991 at the ENT Department of the University of Göttingen, Germany.<sup>30</sup> Iro *et al.* reported a mean five-year survival rate of 66 per cent in 141 patients who underwent transoral laser surgery for supraglottic squamous cell carcinomas (56 per cent for advanced tumour stage T<sub>3</sub> and T<sub>4</sub>) at the ENT

Department of the University of Erlangen, Germany.<sup>31</sup> The comparatively late clinical presentation associated with the frequently observed submucosal tumour growth may play a significant role in the poorer prognosis for malignant sialogenic tumours, compared with the surface-growing squamous carcinomas.

### Conclusion

Local resection into healthy tissue with removal of regional lymph node groups should be the treatment of choice for mucoepidermoid carcinomas and poorly differentiated adenocarcinomas of the larynx. In contrast, for adenoid cystic carcinomas radical surgery may not be indicated due to the high rate of distant metastases, and elective neck dissection is not recommended because of the low incidence of cervical metastases.

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