

# Mucoepidermoid carcinoma of the larynx: report of three cases

DRAGO PRGOMET, MARIO BILIĆ, ŽELJKO BUMBER, SPOMENKA MANOJLOVIĆ\*, VLADO KATIĆ

## Abstract

Mucoepidermoid carcinoma of the larynx is very rare, with only a few individual cases or studies in small patient groups reported in the literature. Treatment modalities for this type of carcinoma are not uniform; in addition, errors in the recognition and pathologic diagnosis are not uncommon. During the period 1991–2000, 771 cases of malignant laryngeal tumours were recorded and histologically verified at the University Department of Otorhinolaryngology and Cervicofacial Surgery, Zagreb University Hospital Centre, three of them were mucoepidermoid supraglottic carcinomas. The experience acquired in the treatment of these tumours is presented along with a review of the literature.

**Key words:** Laryngeal Neoplasms; Carcinoma, Mucoepidermoid

## Introduction

The first description of mucoepidermoid carcinoma dates from 1924.<sup>1</sup> Stewart *et al.* described 45 cases of mucoepidermoid carcinoma of salivary glands and divided them into two groups, benign and malignant, based on the histological and clinical findings.<sup>2</sup> Arcidiacono and Loineo were the first to describe such a tumour of the larynx in 1963,<sup>3</sup> with 80 mucoepidermoid carcinomas of the larynx being reported in the literature to date.

These tumours are believed to develop from ductal elements of the submucosal glands.<sup>4</sup> Their localization depends on the distribution of laryngeal subepithelial glands and intra-epithelial mucous glands. The most common sites include the floor of the laryngeal ventricle, false vocal folds and anterior commissure, whereas the true vocal folds are only exceptionally involved. They often spread submucosally by forming a swelling with an intact mucosal surface, thus decreasing the probability of early detection.

Three patients with mucoepidermoid carcinoma of the larynx out of 771 patients with malignancies of the larynx treated at our Department between January 1, 1991 and December 31, 2000 are presented.

## Case reports

### Case 1

A 55-year-old non-smoking male presented with painful swallowing persisting for three months and hoarseness for the last two weeks. The patient's breathing was normal. A tumour was diagnosed by clinical and endoscopic examination. It was localized on the laryngeal side of the epiglottis and right ventricular fold. The arytenoid was free and vocal fold motility was normal. The tumour was classified as T<sub>2</sub>N<sub>0</sub>M<sub>0</sub> according to UICC criteria.<sup>5</sup> Histological diagnosis was a high grade mucoepidermoid carcinoma (Figure 1). Supraglottic laryngectomy was performed, with access made through the neck and selective lateral dissection on the right side. Tumour excision *in toto* was performed and complete tumour

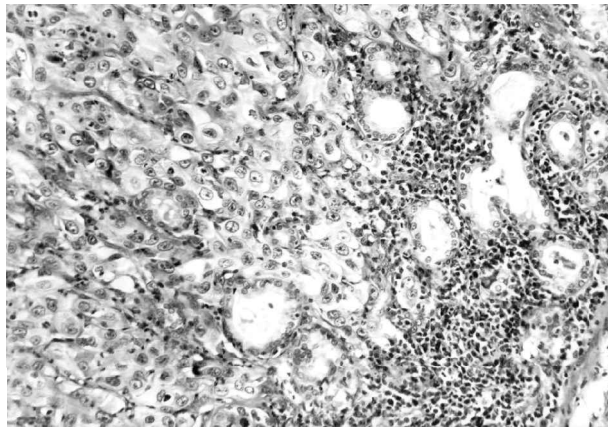


FIG. 1

Mucoepidermoid carcinoma of the larynx (H & E; ×200).

removal was confirmed by frozen section analysis. The dissected portion contained nine tumour-free lymph nodes. Surgery was followed by 30 irradiation fractions (total dose 6000 cGy). Six years post-operatively the patient is disease-free, with normal swallowing and breathing functions.

### Case 2

A 66-year-old female, a smoker who occasionally drinks alcohol, was admitted with signs of hoarseness persisting for six months and laboured breathing during the previous two weeks. A supraglottic tumour of the right side of the larynx was found, with fixation of the right vocal fold. The tumour was classified as T<sub>3</sub>N<sub>0</sub>M<sub>0</sub>. Upon admission, a tracheostomy was performed and squamous cell cancer was diagnosed by biopsy. A total laryngectomy, including bilateral selective lateral and frontal neck dissection (regions I-IV and VI), was performed. The final histological diagnosis was high grade mucoepidermoid carcinoma. Flow cytometry showed aneuploidy (total S phase 9.22 per

From the University Department of Otorhinolaryngology and Head and Neck Surgery, and the Department of Pathology\*, Zagreb University Hospital Center, Zagreb, Croatia.

Accepted for publication: 29 August 2003.

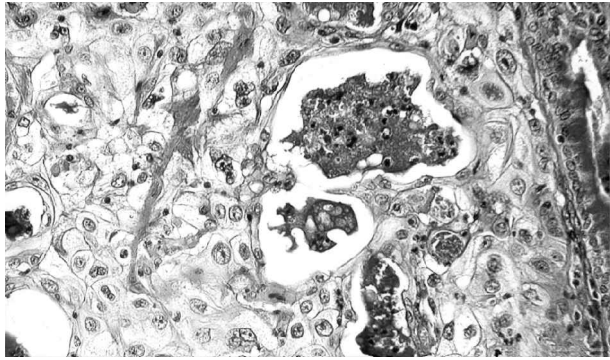


FIG. 2

Mucoepidermoid carcinoma of the larynx (PAS; x200).

cent and a high aneuploid fraction). The dissected portion contained 12 tumour-free nodes. The patient received 30 irradiation fractions (total dose 6000 cGy). Fifty-one months post-operatively the patient is disease-free.

Case 3

A 48-year-old male, a non-smoker, presented with painful swallowing persisting for two months. The tumour involved the laryngeal aspect of the epiglottis and left aryepiglottic fold. A node of 1 cm in diameter was palpable in the neck, ipsilaterally. The tumour was classified as T<sub>2</sub>N<sub>1</sub>M<sub>0</sub>. Histological diagnosis was high grade mucoepidermoid carcinoma. A supraglottic laryngectomy was performed by CO<sub>2</sub> laser and modified radical type III dissection on the left. Tumour excision *in toto* was performed and total removal of the tumour was confirmed by frozen section analysis, which also verified the initial histological diagnosis (Figure 2). The dissected portion contained 15 tumour-free lymph nodes. Sinus histiocytosis and follicular hyperplasia (pT<sub>2</sub>, pTN<sub>0</sub>, pTM<sub>0</sub>) were also present. Surgery was followed by 30 fractions of irradiation (6000 cGy). Thirty-nine months post-operatively, the patient is disease-free, with normal swallowing and breathing functions.

Discussion

Review of the literature yields some 80 instances of mucoepidermoid carcinoma. Their distribution corresponds to the location of salivary glands. Table I summarizes defining characteristics and treatment modalities for mucoepidermoid carcinoma (Table II) from previously published studies.<sup>3,4,6-13</sup> The characteristics of mucoepidermoid carcinomas in our patients were comparable to those reported elsewhere, except for their exclusive supraglottic localization. These tumours are associated with a high rate of misdiagnosis based on biopsy findings,<sup>4,6,9,12</sup> being mostly mistaken for squamous cell carcinoma. One of our patients was initially misdiagnosed too, thus a thorough inspection is recommended and additional analysis of the

TABLE I

CHARACTERISTICS OF MUCOEPIDERMOID CARCINOMA OF THE LARYNX

Characteristic	Cases	
	n	%
Male	44	70
Female	19	30
Age range (yrs)	21-81	
Mean age (yrs)	57	
Localization:		
supraglottic	36	57
glottic	19	30
subglottic	5	8
transglottic	3	5
Metastasis	19	30

TABLE II  
TREATMENT OF MUCOEPIDERMOID CARCINOMA

Method of treatment	n	%
Laryngectomy	21	45
total	10	21
partial	11	24
Laryngectomy + neck dissection	12	26
total laryngectomy	9	19
partial laryngectomy	3	7
Laryngectomy + irradiation	3	7
total laryngectomy	2	5
partial laryngectomy	1	2
Laryngectomy + neck dissection + irradiation	4	9
Total laryngectomy	3	7
Partial laryngectomy	1	2
Irradiation only	6	13
Total	46	100.0

- Mucoepidermoid carcinoma of the larynx is rare
- Misdiagnosis on biopsy material is not uncommon
- Treatment by surgery and post-operative radiotherapy should be dictated by the histological findings and grade of the tumour

preparations thought to be of salivary gland origin. Furthermore, the tumour grade should also be taken into consideration on deciding on the treatment option and prognosis in patients with minor salivary gland carcinomas.<sup>9,14</sup> Some authors make additional use of histological classification on predicting the outcome of major and minor salivary gland carcinomas,<sup>15</sup> whereas others consider the clinical stage of the tumour as the single most important prognostic factor.<sup>16,17</sup> Damiani *et al.* found the classification of laryngeal tumours to bear prognostic significance: using different treatment methods, they recorded a 100 per cent five-year survival in patients with low grade but only 53 per cent three-year survival in patients with high grade mucoepidermoid carcinoma.<sup>8</sup> As the published reports refer to limited numbers of patients with mucoepidermoid carcinoma of the minor salivary glands, additional studies on the prognostic value of classification of these tumours are needed to make any definite conclusion. Some authors emphasize the classification of major and minor salivary gland tumours as an essential element on making therapeutic decisions.<sup>4,13</sup> They recommend that low grade tumours be treated with radiotherapy or conservative surgery. Post-operative irradiation and comprehensive surgical management are recommended exclusively for high grade tumours. In spite of many published studies of laryngeal salivary gland tumours, it is very difficult to find confirmation of these claims.<sup>3,6-13</sup>

The literature review reveals surgery to be the sole therapeutic method in more than two thirds of cases.<sup>3,4,6-13</sup> In our patients, the operative procedure was always performed first. The extent of the procedure was comparable to those used in the treatment of common types of cancer, along with indications for a particular type of laryngectomy, thus partial laryngectomy being chosen in two cases. One of these two patients had indications for open supraglottic laryngectomy.<sup>10,18,19</sup> In the third patient endoscopic surgery was performed by use of the CO<sub>2</sub> laser, as many specialists do in certain cases of squamous cell carcinoma.<sup>20,21</sup> However, there is only one prior report of endoscopic partial supraglottic laryngectomy by CO<sub>2</sub> laser for the treatment of a mucoepidermoid carcinoma.<sup>12</sup>

Since there is a high incidence of local recurrence in cases of high grade mucoepidermoid carcinoma (up to 50

per cent), most authors recommend post-operative radiotherapy.<sup>22</sup> As shown in Table II, only 16 per cent of patients with this tumour received post-operative radiotherapy, whereas it was used in all of our patients.<sup>8,13,22</sup>

While surgery is obviously the treatment of choice, the value of sole radiotherapy in the treatment of mucoepidermoid carcinoma irrespective of localization is questionable. Although mucoepidermoid carcinomas are considered to be moderately radiosensitive, there are six reports of patients who underwent radiotherapy alone, three of them being symptom-free three years after treatment.<sup>4</sup> There is a consensus among authors on the necessity of therapeutic dissection of a clinically positive neck.<sup>23–25</sup> However, the choice of proper treatment method is in dispute in those cases of salivary gland tumours where the neck is clinically negative. Based on the experience with mucoepidermoid tumours of major salivary glands, various authors recommend different procedures: dissection of exclusively first echelon lymph nodes in all tumours,<sup>26</sup> post-operative irradiation of high-risk tumours,<sup>27</sup> and finally obligatory elective dissection in case of high grade tumours.<sup>23–25</sup> We followed the recommendations of those authors who favour elective surgery of the neck in patients with high grade mucoepidermoid carcinoma. In one case we performed a curative, and in another an elective dissection.

The treatment of mucoepidermoid carcinomas has not been standardized due to their low incidence and resultant disagreement. We consider the clinical status and tumour grade to be significant prognostic factors. Our experience suggests that it is possible to preserve the function after the operative procedure, provided there is a free margin and usual conditions are met. Our cases justify partial laryngectomy as well as endoscopic partial laryngectomy by CO<sub>2</sub> laser in selected patients. We recommend elective neck dissection in patients with high grade mucoepidermoid carcinoma. Irradiation is an effective adjuvant therapy for microscopic residual disease in high grade tumours.

We believe that the size and localization of mucoepidermoid carcinoma of the larynx and neck node status should be the primary criteria for the extent of surgery. In addition, the neck procedure and post-operative radiotherapy should be dictated by the pathohistologic findings and histological grade of the tumour.

## References

- 1 Masson P, Berger L. Epiteliomas a double metaplasie de la parotide. *Bull Assoc Fr Etude Cancer* 1924;**13**:366–73
- 2 Stewart FW, Foote FW, Becker WF. Mucoepidermoid tumors of salivary glands. *Ann Surg* 1945;**122**:820–44
- 3 Arcidiacono D, Loineo DG. Tumori muco epidermoidali salivari. *Clin Otorhinolaryngol* 1963;**15**:95–108
- 4 Cumberworth VL, Narula A, MacLennan KA, Bradley PJ. Mucoepidermoid carcinoma of the larynx. *J Laryngol Otol* 1989;**103**:420–3
- 5 UICC International Union against Cancer. *TNM Classification of Malignant Tumors*. 5th edn. New York: Wiley-Liss, 1997
- 6 Alavi S, Namazie A, Calceterra TC, Blackwell KE. Glandular carcinoma of the larynx: the UCLA experience. *Ann Otol Rhinol Laryngol* 1999;**108**:485–9
- 7 Binder WJ, Som P, Kaneko M, Biller HF. Mucoepidermoid carcinoma of larynx. A case report and review of the literature. *Ann Otol Rhinol Laryngol* 1980;**89**:103–7
- 8 Damiani JM, Damiani KK, Hauck K, Hyams VJ. Mucoepidermoid-adenosquamous carcinoma of the larynx and hypopharynx: a report of 21 cases and review of the literature. *Otolaryngol Head Neck Surg* 1981;**89**:235–43
- 9 Ferlito A, Recher G, Bottin R. Mucoepidermoid carcinoma of the larynx. A clinicopathologic study of 11 cases with review of the literature. *ORL J Otorhinolaryngol Relat Spec* 1981;**43**:280–99
- 10 Gomes V, Costarelli L, Cimino G, Magaldi L, Bisceglia M. Mucoepidermoid carcinoma of the larynx. *Eur Arch Otorhinolaryngol* 1990;**248**:31–4
- 11 Hamlyn PJ, O'Brien CJ, Shaw HJ. Uncommon malignant tumours of the larynx. A 35 year review. *J Laryngol Otol* 1986;**100**:1163–8
- 12 Lippert BM, Werner JA, Schluter E, Rudert H. Mucoepidermoid cancer of the larynx. Case report and review of the literature. *Laryngo-Rhino-Otol* 1992;**71**:495–9
- 13 Spiro RH, Hajdu SI, Lewis JS, Strong EW. Mucous gland tumors of the larynx and laryngopharynx. *Ann Otol Rhinol Laryngol* 1976;**85**:498–503
- 14 O'Brien CJ, Soong SJ, Herrera GA, Urist MM, Maddox WA. Malignant salivary tumors – analysis of prognostic factors and survival. *Head Neck Surg* 1986;**9**:82–92
- 15 Goode RK, Auclair PL, Ellis GL. Mucoepidermoid carcinoma of the major salivary glands: clinical and histopathologic analysis of 234 cases with evaluation of grading criteria. *Cancer* 1998;**82**:1217–24
- 16 Anderson LJ, Therikildsen MH, Ockelmann HH, Bentzen JD, Schiodt T, Hansen HS. Malignant epithelial tumors in the minor salivary glands, the submandibular gland and the sublingual gland. Prognostic factors and treatment results. *Cancer* 1991;**68**:2431–7
- 17 Spiro RH, Huvos AG, Berk R, Strong EW. Mucoepidermoid carcinoma of salivary gland origin. A clinicopathologic study of 367 cases. *Am J Surg* 1978;**136**:461–8
- 18 Krajina Z. The Zagreb method of partial laryngectomy: retrospective study 1970–1986. *Acta Med Croatica* 1999;**53**:179–83
- 19 Lutz CK, Johnson JT, Wagner RL, Myers EN. Supraglottic carcinoma: patterns of recurrence. *Ann Otol Rhinol Laryngol* 1990;**99**:12–7
- 20 Rudert HH, Werner JA, Hoft S. Transoral carbon dioxide laser resection of supraglottic carcinoma. *Ann Otol Rhinol Laryngol* 1999;**108**:819–27
- 21 Steiner W. Results of curative laser microsurgery of laryngeal carcinomas. *Am J Otolaryngol* 1993;**14**:116–21
- 22 Garden AS, Weber RS, Ang KK, Morrison WH, Matre J, Peters LJ. Postoperative radiation therapy for malignant tumors of minor salivary glands. Outcome and patterns of failure. *Cancer* 1994;**73**:2563–9
- 23 Armstrong JG, Harrison LB, Thaler HT, Friedlander-Klar H, Fass DE, Zelefsky MJ, *et al.* The indications for elective treatment of the neck in cancer of the major salivary glands. *Cancer* 1992;**69**:615–9
- 24 Ferlito A, Shaha AR, Rinaldo A, Mondin V. Management of clinically negative cervical lymph nodes in patients with malignant neoplasms of the parotid gland. *ORL J Otorhinolaryngol Relat Spec* 2001;**63**:123–6
- 25 Medina JE. Neck dissection in the treatment of cancer of major salivary glands. *Otolaryngol Clin North Am* 1998;**31**:815–22
- 26 Bardwill J. Tumors of the parotid gland. *Am J Surg* 1967;**114**:498–502
- 27 Frankenthaler RA, Byers RM, Luna MA, Callender DL, Wolf P, Geopfert H. Predicting occult lymph node metastasis in parotid cancer. *Arch Otolaryngol Head Neck Surg* 1993;**119**:517–20

Address for correspondence:

Drago Prgomet, M.D., Ph.D.,  
University Department of Otorhinolaryngology, and Head and Neck Surgery,  
Zagreb University Hospital Center,  
Šalata 4,  
HR-10000 Zagreb,  
Croatia.

Fax: +385 1 4920 012

E-mail: drago.prgomet@zg.htnet.hr

D. Prgomet, M.D. takes responsibility for the integrity of the content of the paper.

Competing interests: None declared