

*Originalni članci/  
Original articles*

## ACCESSORY SALIVARY GLAND MALIGNANCIES - REVIEW ON 44 CASES

## MALIGNI TUMORI MALIH PLJUVAČNIH ŽLEZDI - REVIJA 44 SLUČAJA

### Correspondence to:

**Prof. Milan Knežević** MD, DDS,  
PhD, FEBOMS  
University Hospital Insular  
Department of Maxillofacial Surgery

Avda Maritima s/n  
35016 Las Palmas, Spain

Phone: 0034928441700  
E-mail: makmilk@telefonica.net

Milan Knežević<sup>1</sup>, Maria del Carmen Camacho,<sup>2</sup>  
Nebojša Jović<sup>3</sup>

<sup>1</sup>University Hospital Insular, Department of Maxillofacial Surgery,

<sup>2</sup>Department of Anatomic Pathology,  
Avda Maritima s/n, Las Palmas G.C. Spain

<sup>3</sup>Military Medical Academy, Clinic for maxillofacial Oral Surgery and  
Implantology Belgrade, Serbia

### Abstract

The 44 cases found accounted for 39.2% of all minor salivary tumors. The most frequent histological type corresponded to mucoepidermoid carcinoma (MEC), followed by adenocystic carcinoma (ACC) and adenocarcinoma (AC). The prevalent location was the palate for all histological tumor types, mean patient age being in the fourth and sixth decades of life. Women were more affected by MEC and ACC. The highest percentage of recurrence in turns corresponded to ACC.

The differences observed with respect to other published series could be attributed to racial, geographical and/or methodological factors.

### Key words

Accessory salivary glands, malignancy,  
review.

### Ključne reči

male pljuvačne žlezde, maligni tumori, prikaz

## INTRODUCTION

There are a large number (700-1000) of minor salivary glands widely distributed throughout the oral mucosa, floor of the mouth, palate, uvula, posterior tongue, retro molar and peritonsillar area, pharynx, larynx and paranasal sinuses.

Tumors may affect any of these glands, may be benign or malignant and are diverse in their pathology.

Of salivary gland neoplasms, 80% arise in the parotid glands, 10-15% arises in the submandibular glands and the remainder arises in the sublingual and minor salivary glands.<sup>(1)</sup>

About 80% of parotid neoplasms are benign but the relative proportion of malignancy increases in smaller glands - about 50% of submandibular gland neoplasms and the majority of sublingual and minor salivary gland tumours are malignant

Malignant tumors of the salivary glands have an important incidence in head and neck cancer. Although the major salivary glands are most often affected, tumors of the minor glands are of particular interest in view of their direct repercussions upon the oral cavity. In addition, though a certain agreement exists as to the frequency and location of major salivary gland tumors, there is considerable controversy in the case of the minor salivary glands. Thus, the frequency of malignant tumors of the minor salivary glands ranges from 45% to 85% depending on the series<sup>(1)</sup>. This important difference is largely attributed to the type of glands considered, since a number of series include the nasal, paranasal, nasopharyngeal and laryngeal glands<sup>(2)</sup>. According to general considerations of the Armed Forces Institute of Pathology (AFIP)<sup>(3)</sup>, based on a series of international publications, 50% of all minor salivary gland neo-

plasms are malignant. However, geographical variations exist in tumor incidence as a function of histological type and anatomical location<sup>(4-9)</sup>. The data provided by the AFIP<sup>(3)</sup> pertaining to material reviewed since 1985 indicate that 66% of the glandular tumors located in the lower lip, 31% of those affecting the upper lip, and 50% of all palatal growths are malignant. In the case of the tongue, retromolar zone and floor of the mouth, these figures reach 80%, 93% and 93%, respectively.

In one of the most extensive reviews, Waldron et al.<sup>(10)</sup>, found tumors of the minor salivary glands to account for approximately 15% of all tumor processes - including benign, malignant and potentially malignant disease. Of the 326 cases of salivary neoplasms recorded from several services of oral pathology, 57.5% corresponded to benign tumors while 42.5% were malignant - including 132 cases involving the minor salivary glands. In this latter group of glands, upon evaluating the histological type, these authors found mucoepidermoid carcinoma (MEC) to be the most frequent tumor, followed by adenocarcinoma (AC) and adenocystic carcinoma (ACC). In the study of Regezi et al.<sup>(11)</sup>, MEC was likewise the most frequent histological type, respectively followed by ACC and AC. Other authors have reported the same order of frequency, though with different percentages<sup>(3,4)</sup>. On analyzing the data in the literature regarding patient sex, all three of the above histological variants were found to be more common in females particularly AC, with a ratio of 4.6:1. As to age, the highest mean value corresponded to MEC, while similar mean ages one decade younger were recorded for both ACC and AC

In terms of tumor location, the palate was the most commonly affected area<sup>(3, 10-13)</sup>. The description of new histological variants among adenocarcinomas may modify some of these data, however

– particularly as regards ACC. Thus, the latest literature presents series comprising low-grade malignancy polymorphic adenocarcinoma, with the contribution of clinical and therapeutic data<sup>(14-16)</sup>. The present paper is a retrospective study of a large series of malignant tumors of the minor salivary glands pertaining to one same Oral Pathology Diagnostic Center. The frequency of the different histological types was investigated, along with the clinical data corresponding to each. In turn, comparisons were made with the world literature, with the aim of identifying possible geographical and/or populational differences.

## MATERIAL AND METHODS

A data search was conducted in the records of the Department of Maxillofacial Surgery, University hospital Insular, Las Palmas, Spain, comprising the period between 1996 and 2008.

169 minor salivary gland tumors were found, of which 44 corresponded to malignant tumors documented through clinical protocol and histological examinations.

A revision was made of the previous microscopic diagnoses, following the histological criteria and new classification of the World Health Organization<sup>(17)</sup>. Based on the updated diagnoses, analyses were made of the corresponding clinical data, and mean patient age, sex-related frequency and tumor location were determined. Tumor dimensions were moreover considered, along with their clinical, macroscopic appearance, tentative clinical diagnosis and evolution according to the available data.

Classification; malignant tumors are designated high or low grade dependent on their histology.

High grade: Mucoepidermoid carcinoma (grade III), Adenocarcinoma - poorly differentiated carcinoma and anaplastic carcinoma, Squamous cell carcinoma, Malignant mixed tumors and Adenoid cystic carcinoma

Low grade: Acinic cell tumors, Mucoepidermoid carcinoma (grades I or II).

The malignant tumors most commonly affecting the major salivary glands are mucoepidermoid carcinoma, acinic cell carcinoma and adenoid cystic carcinomas. Among the accessory salivary glands, adenoid cystic carcinoma is the most common.

## RESULTS

The 44 malignant tumors recorded accounted for 39.2% of all the accessory salivary gland neoplasms documented. Of these, 21 cases (47.1%) corresponded to MEC, 18 (41.5%) to ACC and 4 (11.2%) to AC. Only one case (0.9%) of carcinoma developing from a pleomorphic adenoma was observed. Both MEC and ACC were more frequent in females, with ratios of 2.5:1 and 1.6:1, respectively. This ratio was inverted in the case of AC, where 60% of all tumors corresponded to males. Mean patient age was 49 years for MEC, 44 years for ACC and 56 years in the case of AC.

The palate was the most affected site in all cases.

The ACC, clinical-macroscopic appearances was reported, most frequently, as nodular and ulcerated vegetative growths, solid and depressible, and exhibiting a whitish color with ochre areas. Tumor dimensions ranged from 3 to 6 cm; radiologically, five cases showed erosion of the orbital floor, cortical insufflations and dental displacement, with pain.

MEC, macroscopic appearance of varied from pediculated and ulcerative, with a reddish-violet color and deformation. Tumor size ranged from 2 to 3 cm.

The AC was exophytic, ulcerated and wine-colored, with dimensions in the range of 2-3 cm, approximately.

The tentative clinical diagnoses prior to biopsy varied greatly. In fact, clinical criteria only coincided with the histopathological diagnosis in 16.2% of the ACC, 13% of the MEC and in 25% of the AC. In the case of ACC, the Test of clinical diagnoses included other salivary tumors such as pleomorphic adenoma and odontogenic tumors such as myxoma. In the case of MEC, 26% were clinically diagnosed as squamous cell carcinoma, 15% as pleomorphic adenoma, and 8% as pyogenic granuloma. The remaining 18.3% comprised highly diverse diagnoses such as mucocele, hemangioma and nonspecific ulcer. In the case of AC, 135% were diagnosed as pleomorphic adenoma and 12.5% as sinus pathology, while the remaining 50% received no tentative clinical diagnosis.

In most cases of ACC (54.5%), tumor evolution was several months, whereas in the case of both MEC (65%) and AC (66%), evolution in most cases extended over years. Management was surgical in all cases. Recurrence, according to the available data, was estimated to be at least 27% (10 cases) for ACC, versus 14.2% (6 cases) for MEC and 11.1% (1 case) in the case of AC. Pulmonary metastases were diagnosed in only one patient with ACC.

## DISCUSSION

Knowledge of salivary gland tumors has grown considerably in recent years, due to improved information on the behavior and prognosis of already classified tumors and the description of new histological variants. The introduction of new tumor types may moreover modify earlier data concerning the relative frequencies and anatomical locations of these neoplasms<sup>(1,3,17)</sup>.

Regarding the differential diagnosis, MEC is the commonest malignancy of the parotid gland and is the second commonest of the submandibular gland (after adenoid cystic carcinoma). It represents about 8% of all parotid tumors. AC represents 2-3% of salivary tumors. ACC is a low-grade neoplasm that represents 1% of all salivary gland neoplasms. 95% arise in the parotid gland.

Regional metastases from skin or mucosal malignancies may present as salivary gland masses. 1-3% of patients with cutaneous squamous cell carcinoma of the head and neck experience metastatic spread to the parotid-area lymph nodes.

Lymphoma can occasionally present in a salivary gland.

## CONCLUSION

The frequency of malignant tumors of the accessory salivary glands in the present study coincides with the observations of other sources in the international literature<sup>(3, 10)</sup>. The differences noticed in various parameters (histology, age, gender and localization of tumor), from some series in literature, are most probably due to geographical variations, and also, maybe, from reference used medical centers. However, on comparing the proportions of each histological type, considerable differences were noted particularly in the case of ACC and in relation to the series of Waldron et al.<sup>(10)</sup>.

### Apstrakt

Prikazano je 44 slučaja malignih tumora, koji čine 39,2% slučajeva svih tumora malih pljuvačnih žlezdi. Najčešći histološki tip malignog tumora malih pljuvačnih žlezdi je bio mukoepidermoidni karcinom, zatim adenocistični karcinom i na kraju adenokarcinom. Najčešća lokalizacija je palatum a životna dob u 4.-oj i 6.-oj deceniji života. Kod žena se češće javljaju mukoepidermoidni i adenocistični karcinom. Najčešće se recidivi javljaju kod obolelih od adenoicističnih karcinoma. Različiti podaci o pojavi malignih tumora malih pljuvačnih žlezdi zavise od referentnosti centara gde se dijagnostikuju, geografske lokacije i histoloških dijagnostičkih procedura

### REFERENCES

1. Seifert G, Brochoeriu C, Cardesa A, Eveson JW: WHO International Histological Classification of Tumors. Tentative histological classification of salivary gland tumors. *Pat Res Pract* 1990;186: 555-81.
2. Eveson JW, Crawson RA. Tumors of minor salivary glands; a demographic study on 336 cases. *J Oral Pathol*, 1985; 14: 500-9
3. Ellis GL, Auclair PL. AFIP, Washington DC. III Series, Fascicle 17, 1996. P 31-3, p 203-4.
4. Eneroth CM. Salivary gland Tumors in parotid, submandibular and palate region glands. *Cancer* 1971;27: 1415-8.
5. Eveson JW, Cawson RA. Salivary gland tumors. A review of 2410 cases with particular references to histological types, site age and sex distribution. *J Pathol*1985; 146-51-8.
6. Seifert G et al. Diseases of salivary glands: pathology, diagnosis, treatment, facial nerve surgery. Stuttgart, New York: Georg Thieme Verlag 1986. P 171-9
7. Spiro RH et al. Mucoepidermoid carcinoma of salivary gland origin: a clinicopathological study of 367 cases. *Am. J. Surg* 1978; 136: 462-8.
8. Sadeghi A et al. Minor salivary gland tumors of the head and neck: treatment strategies and prognosis. *Am J Clin Oncol* 1993; 16: 3-8.
9. Onyango et al. Salivary gland tumors in Kenya. *East Afr Med J* 1992; 69: 525-30.
10. Waldron CA et al. Tumors of the intraoral minor salivary gland: a demographic and histologic study of 4426 cases. *Oral Surg Oral Med Oral Path* 1988; 66: 323-33.
11. Regezi JA et al. Salivary gland tumors, a histologic and immunohistochemical study. *Cancer* 1985; 55: 108 15.
12. Chaudry AP et al. Histogenesis of adenoid cystic carcinoma of the salivary glands. Light and electron microscopic study. *Cancer* 1986; 58: 72-82.
13. Chau MNY, Radden BC. Intraoral salivary gland neoplasms: a retrospective study of 98 cases. *J Oral Pathol* 1986; 339-42.
14. Vincent SD, Hammond H, Finkelstein MW. Clinical and therapeutic features of polymorphous low-grade adenocarcinoma. *Oral Surg Oral Med Oral Pathol* 1994; 77: 41-4.
15. Mitchell DA, Eveson JW, Ord RA. Polymorphous low-graded adenocarcinoma of minor salivary glands. A report of three cases. *Br J Oral Max Surg* 1989; 27 : 494-500.
16. Brocheriou C. Polymorphous low-grade adenocarcinoma of the minor salivary glands. Seven Cases. *Arch. Anat. Cytol Path.* 1992; 40: 60-72.
17. Seifert G, Sobin LH. Histological classification of salivary gland tumors WHO. International Histological Classification of Tumors. 2<sup>nd</sup> ed. New York Springer -Verlag, 1991. p 17-31.