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TUMORS OF MINOR SALIVARY GLANDS  
(A RETROSPECTIVE STUDY)

TUMORI MALIH PLJUVAČNIH ŽLEZDA  
(RETROSPEKTIVNA STUDIJA)

**Correspondence to:**

Milan Knezevic<sup>1</sup>, Beatriz Baez<sup>2</sup> and Gordana Andjelic<sup>3</sup>

**Gordana Andjelic**

Institute for Medical Research, Military  
Medical Academy  
Belgrade, Serbia  
e-mail: gordana.andjelic13@gmail.com

tel/fax. +381 11 2662 722  
cellular. + 381 64 1924274

<sup>1</sup>Faculty of Medicine and Public Health Sciences ULPGC, Hospital  
Universitario Insular, Las Palmas, Spain

<sup>2</sup>Department of Anatomic Pathology, Hospital Universitario Insular, Las  
Palmas, Spain

<sup>3</sup>Institute for Medical Research, Military Medical Academy, Belgrade,  
Serbia

*Ključne reči*

pljuvačne žlezde usne duplje, maligni  
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*Key words*

oral salivary glands, malignant tumors,  
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*Abstract*

A retrospective study of the minor salivary glands malignant tumors recorded over a 21 years period in a single hospital at the Clinic for Oral and Maxillofacial Surgery and the Department of Pathology was conducted.

The goal is to identify all malignant neoplasms among the total series of minor salivary gland classification of the WHO. Clinical data were analyzed for patient age and sex, tumor location and size, clinical and macroscopic forms, possible clinical diagnosis and evolution using the data available in the existing protocols.

The 178 out of 216 analyzed minor salivary glands contained malignant tumors (82.4%). The most common histological type was mucoepidermoid carcinoma (MEC), than adenocystic carcinoma (AC) and adenocarcinoma (A). The prevalent location was the palate for all histological tumor types; mean patient age was between 50 and 60 years. Women were more affected by MC and AC. The highest recurrence rate corresponded to AC.

The differences observed with respect to various series published could be attributed to genetic predisposition, racial, geographical and/or methodological issues.

*INTRODUCTION*

Malignant tumors of the salivary glands are abundant in head and neck cancers. Although the major salivary glands are most often affected, tumors of the minor glands are of particular interest considering their direct repercussions to the oral cavity. In addition, though a certain agreement of the frequency and location of major salivary gland tumors exists, there is considerable controversy of the minor salivary glands affectation. Therefore, 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 neoplasms are malignant. However, there are geographical variations in tumor incidence, histological types and anatomical locations <sup>(4-9)</sup>. The data provid-

ed 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.

*MATERIAL AND METHODS*

The data were obtained in the medical records of the Laboratory of Histologic Pathology of the Pathology Department and Clinic for Maxillofacial Surgery of the University Hospital Insular Las Palmas Spain during the period between 1992 and 2013.

The cohort of patients with salivary gland tumors consisted of 140 women and 76 men. The mean patient age was between 50 and 60 years. Out of 216 minor salivary gland tumors, 178 corresponded to malignant tumors as proved by radiological and histological analysis.

A revision of the previous microscopic diagnosis was made, following the histological criteria and classification of

the WHO <sup>(10)</sup>. Analyses of the corresponding clinical data, the mean patient age, the sex-related frequency and the tumor location were made based on the updated diagnoses. Tumor dimensions were moreover considered, along with their clinical-macroscopic appearance, supposing clinical diagnosis and evolution according to the available data.

### RESULTS

The 178 malignant tumors that were recorded accounted for 82.4% of all the minor salivary gland neoplasms documented, out of which 85 cases (47.75%) corresponded to MEC, 74 (41.6%) to AC, and 18 (10.1%) to A. Only one case (0.1%) of carcinoma developing from a pleomorphic adenoma was observed. Both MEC and AC were more frequent in females than in males, with ratios of 2.5:1 and 1.6:1, respectively. This ratio was inverted in the case of A, since 60% of these tumors were in males. Mean patient age was 48 years for MEC, 45 years for AC and 57 years for patients with A. The palate was the most affected site in all patients.

The clinical-macroscopic appearance for AC most frequently was 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, four cases showed erosion of the orbital floor, cortical insufflation and dental displacement, with pain.

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

Adenocarcinomas were exophytic, ulcerated and wine-colored, with dimensions in the range of 2 to 3 cm, approximately.

The supposed clinical diagnoses prior to biopsy varied a lot. In fact, clinical criteria only coincided with the histopathological diagnosis in 16.2% of the AC, 13% of the MEC and in 25% of the A. In the case of AC, the rest 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, 17% as pleomorphic adenoma, and 9% as pyogenous granuloma. The remaining 17.3% comprised highly diverse diagnoses such as mucocele, hemangioma or nonspecific ulcer. In the case of A, 12.5% were clinically diagnosed as pleomorphic adenoma and 12.5% as sinus pathology, while the remaining 50% had no tentative clinical diagnosis. In most patients with AC (54.5%), tumor evolved in few months, whereas in patients with either MEC (in 65%) or A (in 66%) evolution extended over years. Management was surgical in all cases. According to available data, at least 17 patients (9.6%) had local recurrence: 10 patients (58.8%) with AC, 6 patients (35.3%) with MEC and 5.9% (1 case) with A. Pulmonary metastases were diagnosed in only one patient with AC.

### DISCUSSION

Abundant salivary glands tumors studies have recently considerably increased knowledge about them, due to improved informations on the behavior and prognosis of already classified tumors and description of new histological variants. Waldron et al. <sup>(11)</sup>, in one of the most extensive

reviews 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 426 cases of salivary neoplasms recorded from several services of oral pathology, 57.5% corresponded to benign tumors while 42.5% were malignant - including 181 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 (A) and adenocystic carcinoma (AC). In the study of Regezi et al. <sup>(12)</sup>, MEC was likewise the most frequent histological type, respectively followed by AC and A. 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 A, with a ratio 4.6:1. As to age, the highest mean value corresponded to MC, while similar mean ages one decade younger were recorded for both AC and A <sup>(10)</sup>. In terms of tumor location, the palate was the most commonly affected area <sup>(3, 10-14)</sup>.

The description of new histological variants among adenocarcinomas may modify some of these data, particularly regarding AC. Thus, the latest literature presents series comprising low-grade malignancy polymorphic adenocarcinoma with the contribution of clinical and therapeutic data <sup>(10, 15-17)</sup>. The introduction of new tumor types may actually modify earlier data concerning the relative frequencies and anatomical locations of the neoplasms <sup>(1, 3, 10)</sup>.

The present report is a retrospective study of a large series of malignant tumors of the minor salivary glands in only one Pathology Diagnostic Center. The frequency of the different histological types was investigated, along with the clinical data corresponding to each of them. Parallel comparisons were made to the world literature, with the aim to identify possible genetic predisposition due to the population differences and various habits. The frequency of malignant tumors of the minor salivary glands in the present study coincides with the findings of other centers published in the international literature <sup>(3, 11)</sup>. However, comparing the proportions of each histological type, considerable differences were noted, particularly for AC compared to the results of Waldron et al. <sup>(11)</sup>.

The data of tumor frequency due to patients' age and sex and age were also different in other studies. Therefore, while Waldron et al. <sup>(11)</sup> found all three tumor types to be more common in females, we found A to affect males more than females. Further, the female-to-male ratio for MEC in our study was significantly higher than in the study of the authors mentioned above. In turn, mean ages in patients with AC and MC were markedly lower in our study than in that one of Waldron et al. <sup>(11)</sup>, though very similar to those reported by other centers <sup>(3)</sup>. Although general agreement existed regarding tumor location, significant differences were observed in the percentage frequencies - particularly for MEC and A. In contrast, the percentage of palatine AC coincided with that reported in the comparison study <sup>(11)</sup> and by the AFIP <sup>(3)</sup>.

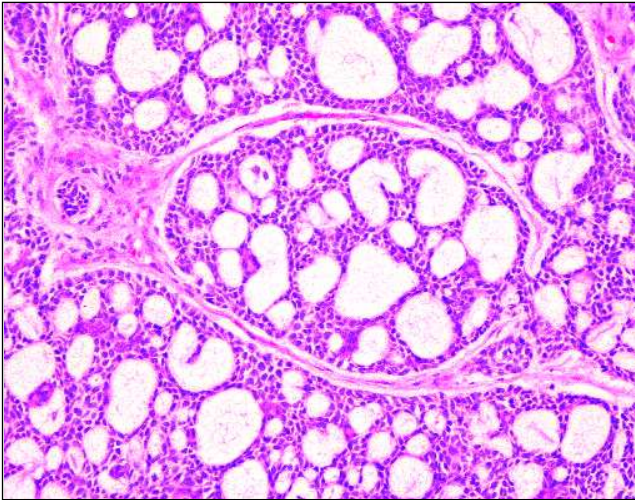
The shortest evolution and highest percentage of recurrence corresponded to AC, with lung metastases being recorded in one patient. The longest evolution and lowest percentage recurrence corresponded to MEC, in agreement with the histological appearance of the tumors, as most were low grade malignancies. Histological grade is the only independent factor affecting survival beyond tumor lymph node metastasis (TNM) staging in salivary gland MEC. Further advances in therapy are needed to improve the outcomes for patients with high-grade lesions (18).

The differences observed in most of the analyzed parameters (hystological type, patient's age and sex, as well as tumor location) with respect to other studies reported in the

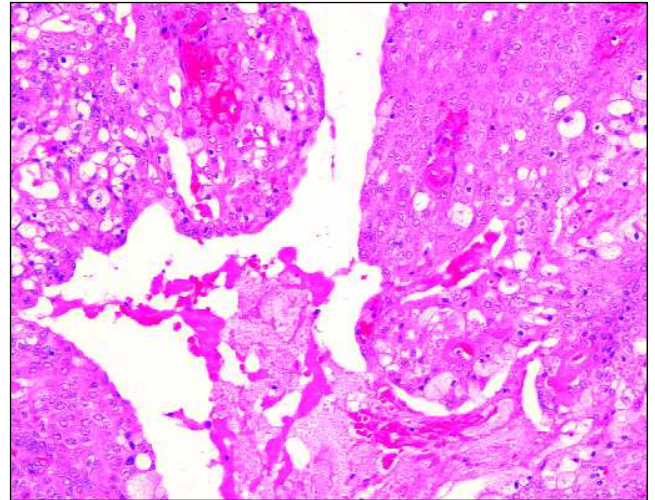
literature may be accounted to the genetic variations in the predisposition to alignant tumors, racial and populational characteristics, as well as different habits in alimentation and hygiene of the patients elsewhere in the world.

*Acknowledgement:*

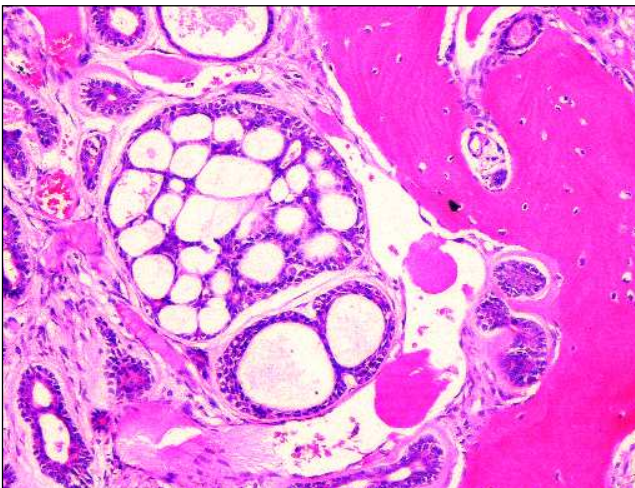
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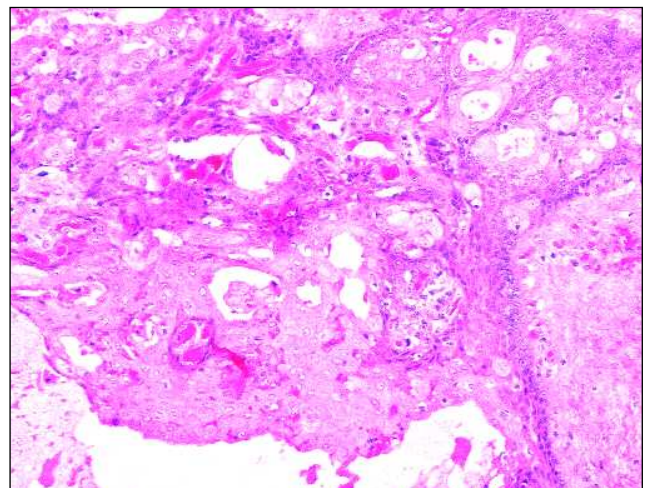
**Fig. 1.** Adenoid cystic carcinoma, cribriform cylindromatous pattern or sievelike microcystic spaces containing mucinous material (HE, 10 x).



**Fig. 2.** Adenoid cystic carcinoma, bone infiltration (HE, 20 x).



**Fig. 3.** Low-grade mucoepidermoid carcinoma, cystic tumor with intermeditated mucinous and clear cells. (HE, 20 x).



**Fig. 4.** Low-grade mucoepidermoid carcinoma, squamous, intermeditated and columnar cells. (HE, 20x).

### Sažetak

U retrospektivnoj studiji su analizirani maligni tumori malih pljuvačnih žlezda sakupljeni tokom 21 godine samo u jednoj bolnici na Klinici za oralnu i maksilofacijalnu hirurgiju i Odeljenju za patologiju. Cilj istraživanja je bio da se identifikuju maligne neoplazme u ukupnom broju malih pljuvačnih žlezda klasifikovanih prema kriterijumima Svetske zdravstvene organizacije (WHO). Analizirani su klinički parametri kao što su godine i pol pacijenata, lokacija i veličina, klinički i makroskopski izgled tumora, mogućnost postavljanja kliničke dijagnoze i predviđanja evolucije tumora korišćenjem podataka dostupnih u postojećim protokolima.

U 178 uzoraka od ukupno 216 analiziranih malih pljuvačnih žlezda su pronađeni maligni tumori (82.4%). Najčešći histološki tip je mucoepidermoidni karcinom (MEC), zatim adenocistični (AC) i potom adenokarcinom (A). Najčešća lokacija za sve histološke tipove je nepce. Prosečno godište pacijenata je između 50 i 60 godina. Kod žena se češće javljaju MEC i AC. Najčešće recidivira AC.

Razlike u rezultatima dobijenim ovom i drugim studijama mogu biti uzrokovane genetskom predispozicijom, rasnim, geografskim i/ili metodološkim razlikama.

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