

ORAL MALIGNANT TUMOURS: A REPORT ON 728 CASES IN CHILE

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ABSTRACT

The objective of this study was to describe the main clinical characteristics and the relative frequency of each type of oral malignancies received at the Oral Pathology Reference Institute (IREPO) of the Faculty of Odontology; University of Chile, since 1975 to 2006.

Studies were performed of 728 cases of biopsies recorded in the IREPO data base with a diagnosis corresponding to some type of Oral Malignant Tumour (OMT) and which counted with all required clinical and demographic data. Histological sections were observed by two oral pathologists with the purpose of confirming the original diagnosis.

61.6% of OMTs were observed in males and 38.4% in females. Patients average age was 65.3 years, and the most frequent localization was the alveolar/gums ridge (20% of the cases) being the squamous cell carcinoma (SCC) the most frequent pathology (58.4%) These results are similar to the frequencies of oral malignancies reported for other countries as to distribution per gender, age, histological diagnosis. Nevertheless, frequency distribution of each of the OMTs is different to that indicated in most publications.

Key words: mouth neoplasms, squamous cell carcinoma, case reports.

TUMORES MALIGNOS ORALES: UN REPORTE DE 728 CASOS EN CHILE

RESUMEN

El objetivo de este estudio fue describir las principales características clínicas y la frecuencia relativa de cada tipo de neoplasia maligna bucal recibidas en el Instituto de Referencia en Patología Oral (IREPO) de la Facultad de Odontología de la Universidad de Chile, entre los años 1975 y 2006.

Se seleccionaron todos los casos registrados en la base de datos del IREPO entre los años 1975-2006 y que correspondieran a algún tipo de Tumor Maligno Oral (TMO) y de los que se contara con todos los datos clínicos y demográficos requeridos. Con el propósito de confirmar el diagnóstico original, los cortes histológicos fueron observados por dos patólogos orales.

El 61,6% de los TMO se presentaron en hombres y el 38,4% en mujeres. La edad promedio de los pacientes fue de 65,3 años y la localización más frecuente fue en las encías/reborde alveolar (20% de los casos), siendo el carcinoma de células escamosas (CCE) el tipo más frecuente de TMO con un 58,4% de los casos. Estos resultados son similares a las frecuencias de tumores malignos orales reportadas en otros países como también su distribución por género, edad y tipo histológico. Sin embargo, la distribución de frecuencias de los diferentes TMO es distinta a la reportada en la mayoría de las publicaciones.

Palabras clave: tumores bucales, carcinoma de células escamosas, reporte de casos.

INTRODUCTION

Because of their morbidity and mortality, oral malignant tumours constitute a public health problem worldwide¹. In frequency, it is placed within the ten types of cancer with greater incidence throughout the world, presenting great differences in its geographical distribution²⁻⁴.

Oral and oropharyngeal malignancies represent approximately 3% of all malignant tumours in males and 2% in females in the United States⁵. Estimations for 2007 indicated that these tumors would amount to 34,360 new cases causing 7,550 deaths in that country⁶.

In Chile, oral cancer would correspond to 1.6% of total cancer cases, reaching a total of 797 cases in

2002, being present mainly in males, over 45 years of age, with a 2.3:1 rate. Deceases due to oral cancer represent 1% of total deaths in our country, meaning a total of 193 deaths, that is, a mortality rate of 1,33/100.000 inhabitants in 2002 due to this cause⁷.

In spite of the advances in surgical techniques, radiotherapy and chemotherapy, survival rates have not significantly improved in decades and prognosis continues to be related to the stage in which the illness is diagnosed⁸. Regretfully, most patients are diagnosed in advanced stages of the illness due to patient delay or professional delay resulting in very poor survival rates^{9,10}.

Although squamous cell carcinoma (SCC) is the most frequent oral cancer^{3-5,7,11} other types of malig-

nancies may be found, among them, sarcomas, adenocarcinomas, metastasis, etc. being some of worse prognosis than SCC.

There are no studies in Chile demonstrating the relative frequency for each of the malignant tumours present in the mouth nor their relationship with the clinical presentation, age range and gender preference. The objective of this paper was to describe the relative frequency of each OMT according to gender, age, localization, clinical appearance and histopathological diagnosis.

MATERIALS AND METHODS

This study considered all biopsies recorded in Oral Pathology Reference Institute (IREPO) data base of the Faculty of Odontology at the University of Chile, between 1975 and 2006, histopathologically diagnosed as some type of oral malignant tumour (OMT).

Only included were biopsies which counted with records of age and gender of the patient, data on anatomical localization of the biopsied lesion and histological preparation and/or tissue included in paraffin block and diagnosed as OMTs, moderate/severe epithelial dysplasia, or *in situ* carcinoma. Cases not included were those coming from foreign patients as well as those which after being histopathologically re-evaluated were diagnosed as a lesion different from an OMT, or those which diagnoses were impossible to confirm due to insufficient clinical data and/or laboratory techniques.

Data collection was done through a revision of the IREPO data base (Microsoft® Access 2003).

Cases were selected by the recorded histological diagnosis, using for the searching process, key words such as carcinoma, sarcoma, lymphoma, myeloma, metastasis and melanoma. Also included were diagnosis of mucoepidermoid tumours, clear-cell tumors, severe, advanced or evident dysplasia; *in-situ* carcinoma, and any other lesion diagnosed as malignant. Demographic and clinical backgrounds for each case were obtained from the same data base, besides the corresponding clinical history number and histological plate.

Localization was recorded pursuant to the International Statistical Classification of Diseases and Related Health Problems 10th Revision Version for 2007 (ICD-10) of the World Health Organization^{12,13}. Observation of the histological sections was performed at the Department of Oral Pathology of the

Faculty of Odontology at the University of Chile, together with two oral pathologists, consultants of that Department, using an Olympus CX21 optical microscope. Histological sections were stained with the routine hematoxiline-eosine technique. The purpose of this new observation was re-evaluating and confirming the histopathological diagnosis for each case and re-diagnosing those lesions recorded as a certain OMT and being re-classified by WHO¹⁴. In those cases in which the hematoxiline-eosine technique was not sufficient to confirm a diagnosis, histochemical and immunohistochemical techniques were applied.

As the totality of immunohistochemical techniques were not available to confirm the diagnosis of Lymphoma, that denomination was substituted by that of "atypical lymphocytic proliferations compatible with lymphoma" (ALP c/w Lymphoma).

Data analysis was performed using descriptive statistics tests, average and standard deviation for quantitative variables and proportions and ranges for qualitative variables. The software used was STATA 8.1.

RESULTS

The final sample comprised 728 OMT cases. In 92,4% of the cases under study, the histological diagnosis recorded in the IREPO data base was confirmed, while in the remaining cases, the histological diagnosis was changed to another OMT variety. The group which received the greater amount of modifications was that of the salivary glands malignant neoplasms, from which 17.8% (23 cases) were re-classified as another type of adenocarcinoma. In addition, from the 25 cases of severe epithelial dysplasia or *in situ* carcinoma, 5 cases were reclassified as invasive squamous cell carcinoma.

From all OMTs, 61.6% affected males and 38.4% affected women, meaning a 1.6:1 ratio. Patient's average age was 56.3 years with a 2 to 99 years range (Table 1).

Localizations more frequently compromised were the alveolar ridge/gingiva and the oral mucosa, with percentages of 20% and 16.9%, accordingly. On the contrary, the least frequent localization was the major salivary glands with 2.5% of the cases (Table 2).

Results of the distribution analysis with respect to OMT diagnosis showed that the greatest frequency

Table 1: Distribution of malignant neoplasm in the oral cavity by age group.

Age Group	SCC	Melanoma	MEC	ALP cc Lymphoma	Metastasis	ACC	SK	Others	Total
0-10	0.41% n=3	-	-	0.41% n=3	-	-	-	0.82% n=6	1.65% n=12
11-20	0.55% n=4	-	0.69% n=5	0.14% n=1	-	-	0.14% n=1	1.92% n=14	3.43% n=25
21-30	0.55% n=4	0.14% n=1	1.1% n=8	0.55% n=4		0.41% n=3	0.82% n=6	1.24% n=9	4.81% n=35
31-40	3.43% n=25	0.14% n=1	1.65% n=12	1.24% n=9	0.41% n=3	0.69% n=5	0.82% n=6	1.65% n=12	10.03% n=73
41-50	4.26% n=31	0.14% n=1	1.1% n=8	1.37% n=10	0.69% n=5	0.82% n=6	-	1.92% n=14	10.30% n=75
51-60	14.84% n=108	0.41% n=3	1.79% n=13	1.51% n=11	1.37% n=10	0.82% n=6	-	3.30% n=24	24.04% n=175
61-70	18.54% n=135	0.27% n=2	0.69% n=5	1.1% n=8	1.51% n=11	0.69% n=5	-	2.06% n=15	24.86% n=181
71-80	12.09% n=88	0.55% n=4	0.69% n=5	0.14% n=1	0.55% n=4	0.14% n=1	-	1.65% n=12	15.8% n=115
81-90	3.16% n=23	0.27% n=2	-	0.27% n=2	0.27% n=2	-	-	0.27% n=2	4.26% n=31
91-99	0.55% n=4	-	-	0.27% n=2	-	-	-	-	0.82% n=6
Total	58.4% n=425	1.9% n=14	7.7% n=56	7% n=51	4.8% n=35	3.6% n=26	1.8% n=13	14.8% n=108	100% n=728

SCC: Squamous cell carcinoma, MEC: Mucoepidermoid carcinoma, ALPcc Lymphoma: Atypical Lymphocitary Proliferation compatible with Lymphoma, ACC: Adenoid cystic carcinoma, SK: Kaposi Sarkoma.

corresponded to SCC, followed by mucoepidermoid carcinoma (MEC) and ALP c/w lymphoma (Table 1). Those presenting very low frequencies were the non-differentiated carcinoma, myeloma, soft and hard tissue sarcomas and other types of malignant salivary gland neoplasms.

Distribution according to gender varies for each type of OMT. A preference for males is observed in most of them, being Kaposi sarcoma exclusive for that gender. For other types of OMTs, such as SCC; ALP C/w lymphoma, metastasis and osteosarcoma, male-female ratio was 2.1:1, 2.1:1, 1.5:1 and 2.5:1, accordingly. On the contrary, adenoid cystic carcinoma (ACC), mucoepidermoid carcinoma (MEC) and melanoma were present mostly in females, the first one with a 1:3.3 ratio and the other two with a 1:1.8 ratio.

Fig. 1 shows the distribution of each OMT according to age. Average age for SCC cases was 62.1 years and for mucoepidermoid carcinoma (MEC),

44.3 years. For ALP c/w lymphoma, metastasis, adenoid cystic carcinoma (ACC) and melanoma, distribution was more heterogeneous; nevertheless, in all of them there is a preference for adults. Osteosarcomas and Kaposi sarcoma present greatest frequencies in lower ages.

Table 2: Distribution by location of all oral malignancies.

Location	n	%
Alveolar ridge/Gingival	179	20.0
Buccal mucosa	151	16.9
Palate	133	14.9
Tongue	129	14.4
Lips	101	11.3
Maxillary bones	91	10.2
Floor of the mouth	88	9.8
Salivary glands	22	2.5
Total	894	100.0

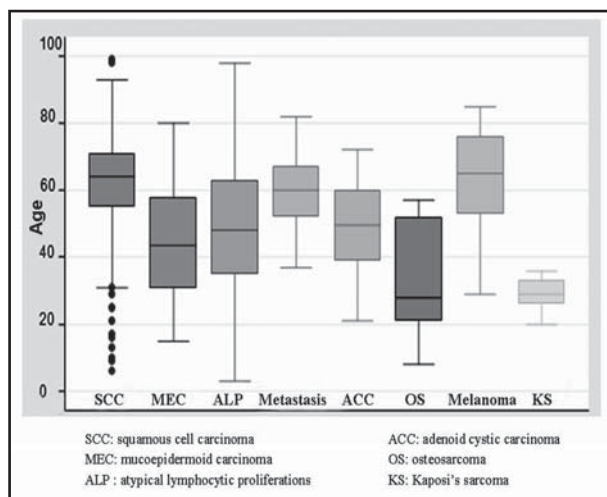


Fig. 1: Age range for each oral malignant tumour. Squamous Cell Carcinoma and Melanoma are frequently seen in older patients. Osteosarcoma and Kaposi's sarcoma are in youngest groups.

Table 3 shows the frequency by site for some OMT (salivary gland excluded). We can see the different distribution related to the type of neoplasm. The SCC is most frequent in tongue but ALP c/c Lymphoma, Metástasis and Kaposi's sarcoma is most frequent in alveolar ridge/gingival. Melanoma is located mainly in the palate.

Salivary gland malignant neoplasms were most frequently present in the minor salivary glands, localization that concentrated 87.4% of those neoplasias. 8.1% was encountered in the parotid gland and 4.4% of the cases of salivary gland malignant neoplasia were found in the submaxilar gland. Minor salivary glands most frequently affected by salivary gland malignant neoplasms were those

located in the palate, area which presented 47.5% of the cases.

The most common salivary gland malignant neoplasia was MEC with 56 cases, that is, 43.3%. The second frequency was adenoid cystic carcinoma (ACC) and the third most frequent salivary gland malignant neoplasia was acinic cell carcinoma, with a 20.2% and a 9.3% of these neoplasias corresponding to each case, respectively.

DISCUSSION

The objective of the study was describing the clinical and demographic characteristics of each OMT and their relative frequency extracted from IREPO data base that counts with a total of 31,479 biopsies recorded during a 32-year period.

Our results show that OMT were most frequently present in male patients, in their sixth and seventh decade of life, preferably localized in the alveolar/gum ridge, and the most frequent diagnosis was that of squamous cell carcinoma. These results are in agreement with other series of published¹⁵⁻²¹, with the exception of the anatomical localization.

OMT frequency was greater in males than in females, with a 1.6: 1 ratio. This tendency is consistent in all studies, in which male-female ratios obtained vary between 1.1:1 in Canada¹⁷ and 6.9:1 in France¹⁶. This tendency of men to develop oral malignant neoplasms is explained by their more frequent smoking and alcohol drinking habits, considered the main hazardous factors for this type of pathologies, data which was impossible to obtain in the present study because it was not recorded in the clinical histories.

Table 3: Frequency of some oral malignancies by location (percentages).

OMN	Location							
	Lips	Other parts of mucosa	Alveolar ridge/gingiva	Palate	Tongue	Floor of mouth	Major salivary glands	Maxillary bones
SCC ^a	16.3	15.8	19.2	7.8	21.7	13.9	0.3	4.9
ALP c/c Lymphoma ^b	3.4	30.5	32.2	18.6	0	1.7	1.7	11.9
Metástasis	0	15.4	33.3	10.3	10.3	2.6	2.6	25.6
Melanoma	0	29.4	23.5	47.1	0	0	0	0
Kaposi's sarcoma	0	6.7	46.7	40	6.7	0	0	0

^a Squamous Cell Carcinoma

^b Atypical Lymphocytic Proliferations compatible with Lymphoma

Similarly, patients average age in all oral cancer cases (56.3 years) coincides with the findings obtained in other countries, ranging from 50 to 65 years^{4,10,11,16-22}. This confirms that oral malignant neoplasms are more frequently present in adults in their sixties and seventies.

The alveolar/gum ridge was the most affected site by some OMTs, followed by the buccal mucosa. This localization differs from that encountered in other researches, where the great majority shows the tongue as main localization. This fact may be explained by the lower frequency of SCC observed in our study in relation to that reported in other series. Our results shows that SCC has, in fact, the tongue as the most affected site, but the present series considers all varieties of oral cancer, many of which are most commonly present in the alveolar/gum ridge. Many others studies consider only oral mucosal lining neoplasm unlike our taking into account all types of malignancies including connective tissue, salivary gland, bone and lymphoid tissue neoplasm. Most reports that show percentages of SCC greater than 85% coincide in that the most common site is the tongue^{10,11,16,18,23}. On the contrary, in those series of cases in which this percentage is lower, the tongue occupies the third or fourth place in the frequency of location^{20,24}.

As mentioned above, squamous cell carcinoma was the most frequently diagnosed OMT corresponding to 58.4% of the cases in this study. This percentage is in close proximity to the work of Han et al.²⁵ from a Stomatology School of China in which SCC occupied the highest proportion with a 53.95%, followed by adenocarcinoma which coincides with the present work. Although, this percentages are lower than most of other series and with the literature regarding its greater frequency in the oral cavity, this percentage is lower than those published by other authors that report frequencies ranging between 65.1%¹¹ and 96%²¹. The lesser frequency of SCC observed in this study may be due to factors such as genetic diversity, exposure to different noxas in the geographic environment, frequency of habits in different communities or due to the different origin of the patients from Dental Schools or General Hospitals. Also should be note that the relative frequency of oral SCC in Chile (1.6%) in relation to all malignant tumours is lesser than reported in others countries. Therefore this situation may to explain the lowest relative frequency of the SCC in this

study but another studies should attempt to explain these differences.

Male-female ration showed variations for each type of oral cancer. For SCC the value was 2.1:1, confirming the relation existing between this type of malignant neoplasia and the associated risk factors, mainly tobacco addiction and alcohol, both more frequent in the male population, however that risk factors were not evaluated in this study. This is in accordance with other SCC series in Latin America that show male predominance close to twice in Venezuela²⁶ Argentina¹⁰ at least in the 1975-2006 period²³ and different from Mexico were no difference was observed²⁷. Male-female ratio for other malignant neoplasm was similar to those published in other studies. The same occurred with the distribution of each type of OMT with respect to age^{17-21,24}. Results of this study show that 87.4% of salivary gland malignant neoplasms occurred in the minor salivary glands. That is complete diverging from other studies²⁸. Nevertheless, this data is biased by the characteristics of IREPO service, as this received a very small amount of major salivary gland biopsies, being these preferably sent to the pathological anatomy services of the hospital where the surgery is being practiced.

From the total number of minor salivary gland malignant tumour recorded, these were most frequently present in the palate, coinciding with other series of similar neoplasms in the United States^{29,30}. MEC was the most common salivary gland malignant tumour, followed by the ACC and the acinic cell carcinoma²⁸⁻³⁰. These frequencies partially coincide with the results published in other series. In Ramoa et al. study²⁹, the most frequent salivary gland malignant neoplasia was the mucoepidermoid carcinoma, followed by the adenoid cystic carcinoma and the low-degree polymorphic adenocarcinomas. Buchner et al.³⁰ reported similar findings; nevertheless, the low-degree polymorphic adenocarcinomas occupied the second place in frequency, displacing the cystic adenoid carcinoma to the third place frequency.

Discrepancies in these results obey to the fact that salivary gland malignant tumours are difficult to diagnose and their classification and diagnosis criteria have been modified along time. Some pathological entities have changed their definition and some new definitions have been introduced. This originates the need of re-diagnosing all salivary gland malignant neoplasms to perform

retrospective studies which may contribute with currently valid data, as it was done, in effect, with the present study.

In Chile, oral cancer is not a mandatory notification disease in the entire country; therefore, there are no complete incidence or prevalence records for this type of cancer. Consequently, the present study contributes with first-hand information with respect to the relative distribution of frequencies of oral malignant tumours.

Retrospective studies using data from hospitals or records supply most useful information. Nevertheless, the validity of their findings varies according to the quality and extension of the collected data³¹. Consequently, conclusions obtained from these data must be carefully handled, being aware of their limitations. The main limitation present in this type of studies is that, when being retrospective, there is no

total certainty that the data recording has been done with the same criterion in all cases. This makes homologation and later data analysis obtained from these records quite difficult.

These results are similar to the frequencies of oral malignancies by gender, age and histological diagnosis reported for other countries. Latin American studies shows not different situation in relation to our results however these are scarce. Researches in Argentina²² and Venezuela²⁶ have found that age, gender and location of oral SCC are similar. This means that the clinical features of oral cancer have not relevant regional differences. Nevertheless, frequency distribution of each of the OMTs is different to that indicated in most publications; maybe ethnic features of Chilean population could explain this result, but this point was not investigated in the present study.

CORRESPONDENCE

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