

Clinical, Epidemiological And Histopathological Prognostic Factors In Oral Squamous Carcinoma

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ABSTRACT The study that was carried out was comprised of 117 cases of oral squamous carcinomas, selected in two years interval, between 2007-2008. The tumors were diagnosed especially at patients between the ages of 50 and 79 years, 96,6% being over 40 years old. It came out a clear predominance of the male sex in approximately 90% of the cases. The main localisation was the lower lip and the tongue (67,5%), in approximately equal proportions (35% and 32,5%). The histopathologically analysis revealed that 37,6% were well differentiated squamous carcinomas, 27,4% were moderately differentiated squamous carcinomas and 35% were poorly differentiated squamous carcinomas. Out of these 3,3% were microcarcinomas, 91,9% were non-metastatic invasive carcinomas and 4,8% were invasive carcinomas with metastatic adenopathy.

KEY WORDS *squamous carcinoma, risk factors*

Introduction

Oral cancers became an important part of oro-maxilo-facial pathology because of its increased frequency, the low rate of survival, as well as the resulted functional or physiognomical defects. The oral carcinogenesis allows the study of the multistadial nature of the cancer. Multiple mechanisms are acting at a molecular level and induce the neoplazic transformation of the squamous cells. At the level of the oral mucosa a continuous lesional spectrum is evidenced having the onset with preinvasive lesions, ending with invasive carcinomas and metastasis (1, 24).

squamous carcinoma is a highly aggressive malignant neoplasia, being sixth as frequency worldwide. It represents almost 95% of the head and neck cancers, predominantly developing in the oral cavity. Annually, there are found about 500000 new cases worldwide. In most cases the affection is diagnosed in an advanced stage, the prognostic being unfavourable. Though the therapeutic progress made in the last years is remarkable the long term rate of survival is still below 50%. The studies have shown a greater incidence among men that chronically exposed themselves to smoking and alcoholism, as well as in families with a history of head and neck cancer (1, 16). There is not yet an explanation for the high frequency of oral cancer in people under 40 years of age that were not exposed to the known risk factors (3, 5, 7, 9, 14,18).

Material and methods

The study is retrospective and was realised by selection of cases that appeared during two years (2007- 2008).

For the retrospective cases the data came from the patients' charts of the Clinic of Oro-Maxilo-Facial Surgery, from the Emergency Hospital's Polyclinic as well as from the Anatomical Pathology Laboratory

The material tissue was processed by classical technique of paraffin embedding. For all cases, there were made seriate sections which were coloured with Hematoxilin-Eosin.

We followed a series of clinical, epidemiological and histopathological indicators like age, sex, pathological antecedents, tumor localization, macroscopical and histopathological parameters.

The integration in the TNM categories was done according to the 2002 TNM classification (15), excepting the cases in which only biopsy was used for diagnosis.

Results

The analyzed squamous carcinomas were present at patients with the age between the third and ninth decade of life. The incidence increase progressively starting with the third decade to the eighth decade of life. Most of the cases (83,8%)

were patients with ages between 50 and 79 years old.

Table 1: Age distribution of cases;

Age groups	30-39	40-49	50-59	60-69	70-79	80-89
Number of cases	4	13	31	45	22	2
%	3,40	11,10	26,50	38,50	18,80	1,7

Regarding the allocation by sex we observed the predominance of tumors in male patients, representing 90% of the cases.

Table 2: Sex distribution of cases;

Sex	Male	Female
Number of cases	105	12
%	89,75	10,25

By anamnesis we pinpointed the risk factors associated with oral carcinogenesis, these being: smoking, alcoholism, family history and pre-existing lesions.

Table 3: Risk factors distribution of cases;

Risk factors	Smoking	Alcoholism	Family history	Pre-existing lesions	Associations
Number of cases	11	7	1	5	21
%	9,40	6	0,85	4,30	18

We observed that mostly the risk factors had associated between them, especially alcoholism and smoking or alcoholism, smoking and pre-existing lesions. If smoking alone or chronic alcoholism alone found themselves in the antecedents of the patients in a proportion of 9,40% and 4,30% , the two associated risk factors were present in a proportion of 18% of the studied cases. The association between smoking and pre-existing lesions was present in a lesser proportion of only 5,55%.

Mostly the risk factors are associated between them. The local pre-existing cancerous lesions were found in 5 cases, isolated or in association with smoking. They are represented by microtraumas, precancerous lesions (erythroplasia, leukoplasmia, lichen planus, oral fibrosis, actinic cheilitis), chronic inflammations of the tongue and lips. The chronic irritations of the oral mucosa (dental malocclusion, dental cavities, defective dentures) and chronic inflammations of the oral mucosa act as a promoter of the oral cancer.

Table 4: Topography distribution of lesions;

Localisation	Lips	Tongue	Soft palate	Gingivae	Floor of the mouth
Number of cases	41	38	5	26	7
%	35	32,50	4,30	22,20	6

Regarding the localization of the lesions, the studied squamous carcinomas had the next

locations in order of the frequency: lips, tongue, gingivae, floor of the mouth, soft palate.

The study indicated the fact that tongue localization, excepting that in the lips, equals all other localizations of the oral squamous carcinomas.

Analysis of morphological parameters were represented by macroscopic appearance and dimensions of the tumors.

The tumors in this study, regarding their type, are classified in the next categories: ulcerate, vegetant, ulcero-vegetant and infiltrative.

Table 5: Macroscopic types of squamous carcinomas;

Macroscopic appearance	Ulcerate	Vegetant	Ulcero-vegetant	Infiltrative
Number of cases	48	31	24	14
%	41	26,50	20,50	12



Figure 1: Lower lip vegetant carcinoma;

The analysis of the tumor dimensions indicated important variations about their maximum diameter. In a decreasing order of frequency we found 31 cases (48,8%) of tumors with dimensions between 2-4 cm in the long tumoral axis and a number of 15 cases (23,4%) of tumors with dimensions over 4 cm in the long tumoral axis. In 4 of the studied cases the tumors were over 4 cm in the long axis with profound invasion through the cortical bone to the floor of the mouth and tongue.

Table 6: The tumoral mass dimensions;

Dimensions	≤ 2 cm (T1)	2-4 cm (T2)	≥ 4 cm (T3)	≥ 4 cm (T4)
Number of cases	11	31	15	7
%	17,20	48,40	23,40	11

The histopathological study had in view the variety of the squamous carcinomas and the degree of differentiation, the tumoral progression stage and the presence of malignant residual cells in the surgical safety borders.

Corresponding to the differentiation degree, the analysis of squamous carcinomas are well differentiated in 44 cases, moderately

differentiated in 32 cases and poorly differentiated in 42 cases.

Table 7: The differentiation degree of tumors;

Differentiation degree	Well differentiated	Moderately differentiated	Poorly differentiated
Number of cases	44	32	42
%	37,60	27,40	35

In the well differentiated squamous carcinomas group were included the keratinized forms of tumors and the verrucous carcinomas. In the moderately differentiated squamous carcinomas group were included the non-keratinized forms and the adenoid variant. In the poorly differentiated squamous carcinomas group were included some non-keratinized forms, the basal and spindle-shaped carcinomas.

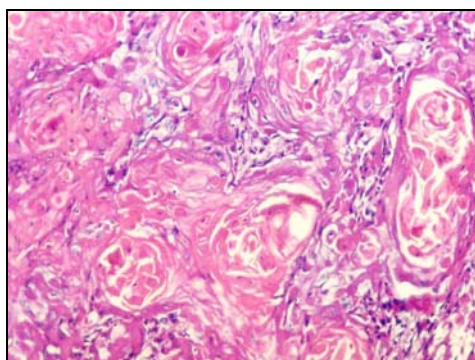


Figure 2: Well differentiated squamous carcinoma in the upper lip, Ob.4, HE stain;

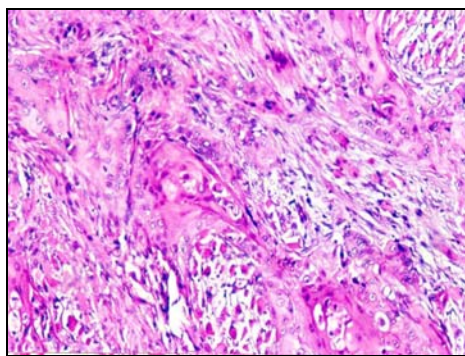


Figure 3: Moderately differentiated squamous carcinoma in the upper lip, Ob.4, HE stain;

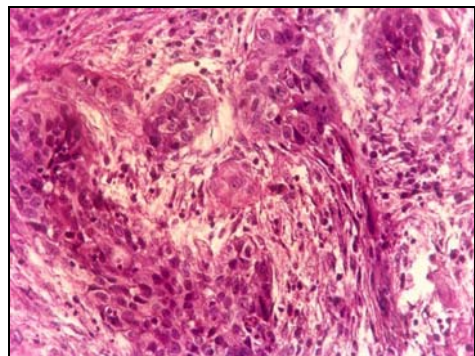


Figure 4: Poorly differentiated squamous carcinoma in the upper lip, Ob.10, HE stain;

Regarding the stage of tumoral progression the analyzed squamous carcinomas correspond to: microcarcinoma in 2 cases, invasive carcinomas in 57 cases and invasive carcinomas associated with metastatic adenopathy in 3 cases.

Table 8: The stage of tumoral progression;

Tumoral progression stage	Microcarcinoma	Invasive carcinoma, no metastases	Invasive carcinoma with metastatic adenopathy
Number of cases	2	57	3
%	3,3	91,9	4,8

Microcarcinomas were localised in the lower lip, associated with modifications of actinic cheilitis and at the tongue associated with aspects of leukoplasia, simple dysplasia and mycelium deposits. Their microscopic aspect was that of a malignant cancer proliferation with minimum invasion of the superficial chorion with the shape of a spur made up of atypical squamous cells.

Frank invasive carcinomas without metastatic adenopathy represent the most frequent neoplasms encountered in this study. Regardless of the histopathological form and of the degree of differentiation the tumors have evolved infiltrative and destructive as islands and neoplastic lobules in the structures of origin.

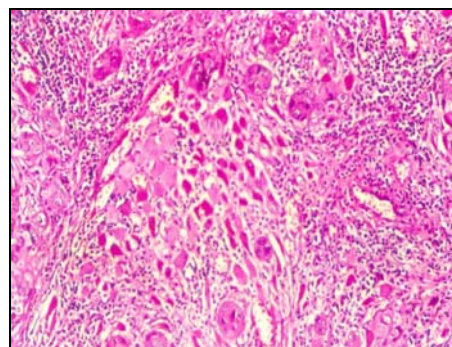


Figure 5: Tongue squamous carcinoma, keratinized form, round island neoplastic invasion, Ob.10, HE stain;

Frank invasive carcinomas with metastatic adenopathy were present in 3 cases. In two cases the metastases were present in one ipsilateral lymph node. In one case the metastases were present in three ipsilateral lymph nodes. The histopathological aspect of the metastases was similar to the one of the primitive neoplasms regarding the tumors shape and degree of differentiation, specifically of non-keratinized squamous carcinomas with moderate or poor degree of differentiation.

Another microscopic parameter that was analysed was represented by the presence of residual malignant cells in the surgical safety

borders. A number of 12 cases did not present an invasion at this level, meanwhile in another 13 cases the invasion was present, taking the form of microcarcinoma in 10 cases and of invasive carcinoma in another 3 cases.

Table 9: The presence of residual malignant cells in the surgical safety borders;

Resection limits	Healthy	Tumoral invasion
Number of cases	12	13
%	48	52
Resection limits	Healthy	Tumoral invasion
Number of cases	12	13
%	48	52

Discussions

In Europe and Australia the incidence among the annually diagnosed neoplasms is 5% compared to Asia and India where it represents almost 50%. In France oral cancers are the most frequent type of cancer for the male patients and is ranked second for causes of death by cancer. Research carried out in Finland between 1953 and 1999 indicates a number of 17383 new cases, mostly in male patients (17, 22).

In the study we carried out most of the analysed cases (83,8%) were comprised between 50 and 79 years. Similar studies show that the predilection age for oral cancer is between 50 and 70 years, the mean age being 64 years. 95% of the diagnosed patients were over 40 years old (11). The frequent development is among men over 50 years. Lately it is observed a rise in the incidence of lesions in women and young people, cases being described even in children patients, especially with tongue localization (3, 5, 7, 9, 14,18).

The data from the specialized literature estimates that the male sex is affected in a proportion of 75-80% of cases, emphasizing that in the last years there was a rise in the incidence of these lesions among female patients. The patients in our study are in terms with these data, 89,75% being male patients.

The American Society of Oncology estimates that in 2004 oral and pharynx neoplasms represented 3,2% and 1,7% of the new cases in male and female patients. In Great Britain oral cancers are ranked 15-th in all male cancers and 20-th in female cancers. World wide , oral cancer represents the fourth type of cancer in male patients and sixth type in women patients (6, 8, 13, 23).

Smoking and alcoholism are dominant risk factors, being found in the past history of 75% of the patients with oropharyngeal and oral cavity cancers (1). It has been observed a frequency of 2-

4 times greater of squamous carcinoma in smokers, the risk rising up to 6-15 times in association with chronic alcoholism (10, 12, 21). Epidemiological studies showed a high risk for this disease for the families with a history of head and neck cancer (9). In this study we observed the fact that most often the risk factors have associated among them, especially alcoholism and smoking, or alcoholism, smoking and pre-existing lesions.

Approximatively 30-35% of the tumors have a tongue localisation, 20-25% a gum localisation, 5-7% are localised on the floor of the mouth, 4-6% on the soft palate and only 2-3% are set on cheeks (11). Our study showed the fact that the tongue localisation, excepting the one on the lips, equals all other localisations of the squamous carcinomas that appear in the oral mucosa. In Great Britain the most common setting is on the floor of the mouth and tongue. In India the most affected area is the oral mucosa, being the consequence of smoking and betel chewing habit. (2, 19). The found aspects, regarding the macroscopic pattern and the tongue malignant tumors are being quite similar to the data mentioned in the literature. Thus it is mentioned that the most commonly met form of this tumor is the ulcerate one, and rarely it can be seen in it's other aspects: vegetant, ulcero-vegetant or infiltrative.

Among the analysed histopathological factors it is considered that the tumor pattern in the tumor invasion front can be one of the prediction factors of tumor evolution. String-shaped or non-cohesive islands or even isolated neoplastic cells invasion can be associated with metastasizing risk growth, though the tumors with a compact aspect in the advancement front are associated with a much less aggressive evolution (18). Also, many studies carried out on the factors of prediction of the evolution of oral squamous carcinomas have as subject the role of the regional metastatic nodes. The presence of metastases in two or more regional lymph nodes, especially associated with extracapsular tumor extension, are a major factor in the unfavourable influence of the prognosis (19).

In the same way, the presence of malignant residual cells in the surgical safety borders has made the subject of numerous studies, being correlated with the tumor progression and with the rate of tumor recurrence. Together with the presence of regional lymph nodes metastases they represent a factor of unfavourable prognosis (20).

Conclusions

The study of the 117 cases of squamous oral carcinomas indicated the predominance of the tumour to men (90%), most of the cases being diagnosed to the age groups between 50 – 70. The most frequent associated risk factors were smoking and alcohol, as they are present in the history of ¾ of the studied cases. The dimension of the tumours, the invasion pattern, the presence of metastasis and the invasion of the safety surgical limits are the most important histopathological prognostic factors.

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