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ORIGINAL ARTICLE

Frequency and histoclinic pathology of malignant and potentially malignant disorders of oral cavity in Chile

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Abstract:

Introduction: Oral squamous cell carcinoma (OSCC) is the sixth most common type of cancer worldwide. Oral potentially malignant disorder (OPMD) represents a tissue where is more probably to occur a cancer in comparison with the apparently normal counterpart. Objective the purpose of this study was to determine the frequency and histoclinicpathology of these diseases in a Chilean population. This was a descriptive retrospective study. **Material and Methods:** Patients diagnosed with DPMO, OSCC and verrucous carcinoma (VC) treated in the Oral Medicine Clinic of University of Chile between 2005 and 2015 were selected, being revised the medical records and histopathological diagnoses. **Results:** From a sample of 241 patients, 60% were women and the mean age was 58 years. The prevalence of DPMO was 15%. The most prevalent of them was oral lichen planus (45%) follow by a 36% of leucoplakias, 16% of actinic cheilitis and 3% of erythroplakias. OSCC and VC accounted to 3.4% and 0.5% of the sample, respectively. The disease-free survival in 5 years for patients with OSCC was 39%. **Conclusions:** The results were similar to those reported by national and international studies must survival found was lower than reported.

Keywords: Mouth Neoplasms; Precancerous Conditions; Chile.

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity. It corresponds to a malignant and invasive squamous pluristratified epithelium and can cause local destructive proliferation and distant metastasis. Malignization is a sequential process, due to an accumulation of genetic and epigenetic alterations and a consecutive exposure to carcinogens[1].

The risk factors more associated with the disease are the use of tobacco, alcohol abuse, low consumption of fruits and vegetables and low socioeconomic status. It is more common in men over 45 years in most of the ethnic groups[2]. Most prevalent locations in the oral cavity is the tongue, followed by the floor of the mouth, gingiva and palate. Lymph node metastasis is considered the most important predictor survival rate, decreasing it near a 50% when there are nodal metastases. Identifying potentially malignant lesions is essential to prevent progression to OSCC.

An oral potentially malignant disorder (OPMD) is a tissue where is more probably to occur a cancer in comparison with the apparently normal counterpart. OPMD can be classified as leukoplakia, erythroplakia, actinic cheilitis (AC) and oral lichen planus (OLP) among others[3]. Histologically, they may have different pathological states, which vary from hyperkeratosis, hyperplasia, atrophy, dysplasia and carcinoma *in situ*. Dysplasia is histologically term defining the epithelial malignant change, characterized by a combination of cellular and architectural changes indicative of a disorder of the epithelial maturation and cell proliferation. These changes are observed in a gradual transition to malignancy. The severity of dysplasia is considered a predictor of progression of OPMD[3]. Risk factors of OPMD are similar to the risk factors of OSCC, however, a large proportion of cases occur in the total absence of any identifiable risk factors[4].

Oral and pharyngeal carcinomas can be associated with significant morbidity, as these cancers and treatments can be disfiguring and can affect daily functions, negatively affecting life quality. The 5- and 10-year survival rates are low: 56 and 41% respectively and have remained relatively unchanged for the past three decades, probably because of late recognition of the disease as it happens in Chile[5]. Consequently, there is an increasing emphasis on early diagnosis and close monitoring of pre-cancerous lesions. Chile has not a registry regarding oral cancer incidence in national level. However, regional archives have started in cities such as Valdivia (1993), Antofagasta (1998) and Concepción (2003)[6].

The identification and characterization of these lesions is essential at national level to address the problem of the OSCC from preventive point of view, which would improve the execution of public policies and, ultimately, improving survival rates and life quality. For this reason, the objective of this study was described the frequency and histoclinicpathology of malignant and potentially malignant disorders of oral cavity in Chile in a dental service representative of the Chilean population.

MATERIAL AND METHODS

This study was retrospective and descriptive and all the samples were included within the ethics statement from project FONDECYT nº 11140281. Any information regarding these study patients remained in complete confidentiality respecting the principles of the Declaration of Helsinki for research with human beings.

It corresponds to a sampling rate non probabilistic for convenience. From the total of patients registered in the database of Clinical Oral Medicine of the Faculty of Dentistry at the University of Chile treated between January 2005 and October 2015 were included those with clinical diagnosis of leukoplakia, erythroplakia, actinic cheilitis, oral lichen planus, oral squamous cell carcinoma and verrucous carcinoma according to the WHO protocol[7].

Variables studied

Data was obtained from the records of selected patients including age, sex, clinical and histopathologic diagnosis, personal medical history, family history of cancer, smoking, alcohol consumption, global symptomatology, evolution time, type of fundamental lesion, location, size, number of lesions, surface, borders, boundaries, color, survival time of cancer patients and cause of death.

Data was pooled clinically in OPMD (leukoplakia, erythroplakia, actinic cheilitis and oral lichen planus) and cancer (squamous cell carcinoma and verrucous carcinoma). For information regarding survival and death date of patients diagnosed with OSCC and verrucous carcinoma, the Civil Registry of Chile was checked. Histopathological diagnoses were obtained from the report of the biopsies that were conducted according to the WHO protocol.

Statistical analysis

Data were analyzed using descriptive statistics. The data were expressed as mean and standard deviation. An exploratory data analysis was performed by Shapiro Wilk normality test. The t-student test, chi-square and ANOVA were used to analyze significant differences between the study variables. It was considered that there are significant differences if p-value <0,05 analyzed with STATA® software.

RESULTS

Out of 1263 patients with a clinical diagnosis of lesions of oral mucosa, 241 presented clinical diagnosis of leukoplakia, erythroplakia, actinic cheilitis, oral lichen planus, OSCC and verrucous carcinoma. The selected biopsies (n=241) corresponded to 19.1% of oral mucosa lesions studied at the Clinical Oral Medicine of the Faculty of Dentistry at the University of Chile. 60.2% (n=145) was women and 39.8% (n=96), men. The mean age was 57.7 years (SD: 15.03). 190 cases were OPMD and 51 were cancer. 85 cases (35.2%) were oral lichen planus, 68 (28.2%) leukoplakia, 31 (25%) actinic cheilitis, 6 (2.5 %) erythroplakia, 44 (12.9 %) OSCC, and 7 (2.9%) verrucous carcinoma (Figure 1).

Leukoplakia, OLP and CV were more prevalent in women (51%, 82% and 86%, respectively). Erythroplakia, AC and OSCC were more prevalent in men (67%, 61% and 55% respectively). The mean of age was 55 (SD: 13.25) 47 (SD: 6.15) 57 (SD: 12.67) 55 (SD: 15.39) 64 (SD: 15.66) and 79 (SD: 8.4) for leukoplakia, erythroplakia, AC, OLP, OSCC and VC, respectively. Only diagnosis of leukoplakia showed statistically significant differences in age of presentation between men (61.6) and women (48.7) (p=0.0001).

OPMD diagnoses are concentrated between 50 and 59 years old corresponding to 27% of cases (n=51). The highest frequency of leukoplakia and OLP was between 50 and 59 years old (n=20.3% and 27% n=23, respectively) for erythroplakia between 40 and 49 years (n=3.5%) and for AC, between 60 and 69 years (n=11, 35.5%). Regarding the distribution according to age range for both OSCC and VC, diagnoses were concentrated among 70-79 years old, corresponding to 27.5% of cases (n=14) (Figure 2).

Regarding systemic diseases, 60.5% of patients with OPMD (n=115) had at least one. The most prevalent disease was hypertension with 34% (n=54), followed by diabetes with 13.2% (n=25). The OPMD with the highest percentage of systemic disease was OLP with 67% (n=57) presenting statistically significant differences compared to

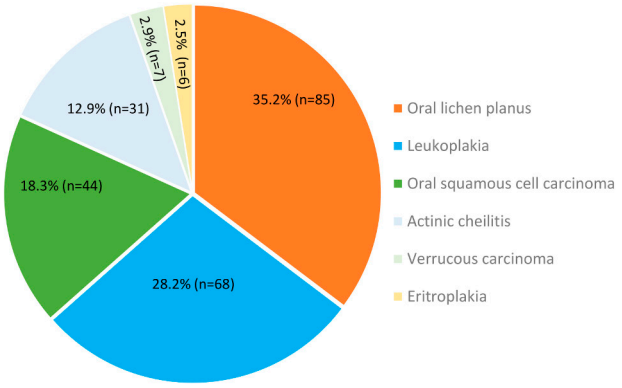

Figure 1. Distribution of percentages of malignant and potentially malignant disorders.

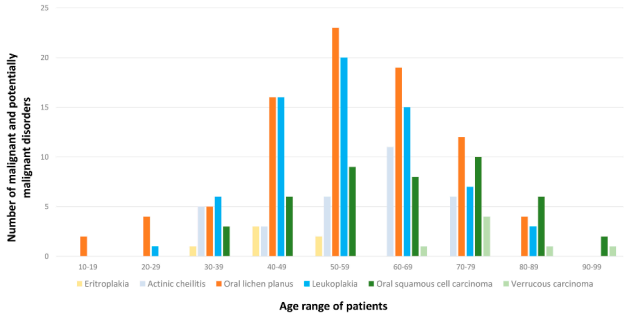

Figure 2. Distribution of number of OPMD and malignancies by age range.

the other diagnoses (p=0.011). The most common disease in OLP was depression with 13% (n=11). In the group of patients with cancer, 27% (n=14) had hypertension. Among family medical history in patients with OPMD, 23% (n=44) had a history of cancer, while in the group of cancer, 11.8% (n=6).

Tabaco and Alcohol

42% of the patients (n=80) with OPMD were smokers. A 26% (n=49) were light smokers (1–39 cig/week). A 34% (n=49) of women and 28% (n=27) men did not smoke. Leukoplakia was the OPMD with most smokers (68%) with significant difference (p=0.001) and in this group, 37% (n=25) was heavy smoker. Respect the association of tabaco with cancer, the percentages of smokers and nonsmokers in this group were similar (29%; n=15 and 31%; n=16, respectively). In 25% of cases (n=13) this information was not informed. A 34% (n=15) of patients with OSCC were smokers.

As for alcohol, in the group of OPMD, a 35% (n=66) did not drink alcohol. In the group with cancer, 18 patients (35%) did but no significant difference was found (p=0.498).

Clinical characteristics of potentially malignant and malignant disorders

45% of the OPMD were asymptomatic. In 55% of OPMD, time evolution of the injury was unknown, except for OLP. Specifically, the group with diagnosis of leukoplakia was mainly located in gingiva (43%), erythroplakias in tongue (50%) and OLP in mucosa (73%). OPMD were mostly diagnosed as single lesions (37%), except OLP, which was multiple (55%). Both leukoplakia and erythroplakia had a mean-size less than 2 cm.

In the group of malignancies 63% presented symptoms and the evolution time was less than or equal to 1 year in 78%. 65% of lesions were ulcers and 27% were tumors. In terms of location, 39% was presented in gingiva, 35% in tongue, and 20% on the palate. Specifically, OSCC was located mainly in gingiva (40%) followed by tongue (39%). VC was located equally in mucosa and palate (43%). Surface of OSCC was mainly homogeneous (34%) and VC was irregular in 86%. The color of OSCC lesions corresponded mainly to red (32%).

Association of clinical and histopathologic diagnoses of the study sample. OPMD histological diagnoses coincided with the clinical diagnosis in 97% of cases. Out of the total number of biopsies performed in cases of erythroplakia and leukoplakia, 51% of them showed dysplasia. Regarding to cases of OLP a 75% (n=24) was histologically compatible with OLP, a 6% (n=2) corresponded to mild dysplasia, and a 9% (n=3) diagnose of epithelial hyperplasia and hyperkeratosis. A 59% (n=112) of all lesions diagnosed as OPMD had not biopsy and for this reason the patients did not attend controls. From all patients with clinical diagnosis of malignancy, 96% (n=49), corresponded histologically with OSCC.

Overall survival of patients with cancer of the study sample. From all patients with malignancies, 43% (n=22) was alive and a 57% (n=29) had deceased. Of the total number of deceased patients, 79% (n=23) died due OSCC, 14% (n=2) died from other causes and in a 14% (n=4) no information was available about cause of death. 40.5% (n=15) died before 2 years from the date of diagnosis and 21.6% (n=8) died before 5 years. Specifically, the 5-year survival for OSCC was 38.7% (n=12) and for VC was 33.3% (n=2). Five years of survival was determinate in a 35% (n=7) of women and a 41.2% (n=7) of men. The average survival time was 3.6 years.

DISCUSSION

We analyzed the frequency and clinical characteristics of 241 patients diagnosed with OPMD and malignancies in the Faculty of Dentistry at the University of Chile between the years 2005-2015. Our clinic represent the greatest area of Santiago de Chile, where live almost the half of the population from the whole country, representing a vast socioeconomic status.

The prevalence of OPMD studied was 11.2%, coinciding with reported frequencies ranging between 0.2% and 13.7%[8,9]. The leukoplakia was found in 4%, similar to that described in the literature where it has been reported prevalence's between 1% and 5%[10,11]. Actinic cheilitis had a 1.8% of prevalence and the erythroplakia a 0.35% which coincides with that reported data by other authors, varying from 0.02% to 0.83%[11,12].

OSCC was the third most frequently diagnosed lesion, representing 3.5% of total lesions of oral mucosa. VC corresponded to 0.4% of diagnoses of the OPMD similar with the low prevalence reported by other authors[13]. When comparing the prevalence of OSCC with any OPMD we can observe that OSCC was diagnosed even more prevalent than OPMD. It is important to emphasize this because possibly, lesions are diagnosed at later stages.

As for the distribution of OPMD by sex, 63% of the total were women what is not in relation to what has been reported worldwide, where described to be more prevalent in men[3,11]. One reason could be due the majority of the patients in clinics in Chile are women, who are prone to present higher self-care status. This may also explain why in our study, women had a higher prevalence of leukoplakia, different from results found in other studies[14].

Actinic cheilitis was found to be mostly diagnosed in men, with a ratio male-female of 1.6:1. This value is much lower than found in other countries[15] but still similar to one study performed previously in Chile[16]. The erythroplakia was mainly diagnosed in men, corresponding to the male-female ratio of 2:1 similar as reported for this lesion[3]. OSCC was diagnosed in 55% in men and VC occurred mainly in women, similar with a reported in Spain (57%)[17].

However, studies indicate that VC affects more men than a women[13]. Regarding age, the average OPMD presentation in our study was 55 years. The literature reports that these lesions occur mainly after 40 years[18]. For example leukoplakia, the average age found in our study was 55 years old, agreeing with previously reported data, which fluctuates between 40 and 60 years[14].

The average for OSCC was 64 years old, similar to that reported in the literature, which concentrates prevalence between 60 and 80 years old[19]. In VC the largest number of diagnoses occurred in the eighth

decade, similar to that reported in Spain[17] but differs from other studies indicating that the VC mainly affects patients between fifth and seventh decade[13].

Several studies establish a strong association between use of tobacco and development of OPMD[10]. In our study, 42% of those with OPMD were smokers and 6% stopped smoking after diagnosis. The consumption of tobacco was 49% in men and 33% in women, indicating that in Chile, there is a higher percentage of women that are smokers compared to other populations, which could influence the higher prevalence of OPMD in women in this studio. The leukoplakia was mainly diagnosed within patients with tobacco habits, which is related to the literature where leukoplakia is six times more prevalent in smokers[10]. It is noteworthy that the presence of leukoplakia in nonsmokers patients (idiopathic leukoplakia) is a risk factor of malign transformation[18].

The most affected anatomical site of OPMD was inside of his cheek, influenced by the high percentage of patients with OLP. In leukoplakia the most affected site was gingiva, followed by tongue and mucosa, This results differs to studies that reported the inner cheek as the most frequent anatomical location[22]. In Erythroplakia the most affected site was tongue (50%), opposing to previously published data where it was established that the main locations were palate and floor of the mouth[12]. In OSCC, the most frequent clinical forms observed were ulcers followed by tumor possibly because diagnoses are made in advanced stages. The most affected site was gingiva (40%) and tongue (39%) different of related by Siegel et al.[23] who proposed tongue as the most affected area.

As for the size of the OPMD, our study showed mostly lesions were smaller than two centimeters, which has clinical implications. Several studies have pointed that OPMD greater than 2 cm are risk factor for malignant transformation[18].

OSCC clinical diagnoses agreed up to 95% with histopathological diagnosis that can be due it is diagnosed in later stages when the clinic is very evident. In leukoplakia, the highest percentage of histological diagnoses corresponded to dysplasia. Studies indicate that approximately 20% of leukoplakia presents dysplasia[24].

Survival rate in our study for OSCC patients for 5 years was 39%. When comparing our study with other reports in Chile, authors reported a survival rate ranging from 46% up to 58.4% at 5 years[19]. Analyzing survival rate by sex, we have observed similar rates between women and men (36% and 41%, respectively) which is not clearly different from what was previously described[25].

One of the causes that could explain the low survival of the patients with OSCC in Chile is the high percentage of smokers and the early age of habit initiation[26]. Chile has the highest prevalence of cigarette smoking among students around the world. One study, which included 44 countries, showed that the monthly smoking prevalence was 32.8%, higher than in most other countries[27]. Another possible cause could be that patients indicate lower alcohol consumption than the real habits

One of the main limitations of this study could be the different criteria of the dentists to make patient's records because there were different professionals carrying out the registers within the last 20 years ten years. Despite that limitation, we stress the importance of having an analysis of prevalence and characteristics of OPMD, OSCC and VC in Chilean patients considering the limited records that exist.

It is necessary that chilean population to make diagnosis in the initial stages of the disease to improve the survival of those affected. A study in Taiwan, for example, states that the patients who were treated after 120 days after diagnostic had a higher risk of death when compared to those treated after 30 days[27].

The main clinical importance of studying OPMD and malignancies is know the prevalence and survival in this kind of lesions in Chile to contribute to the generation of a national registry for oral pathologies and in this way, intervene in the population's preventive plans to prevent the development of OSCC and increase the survival of those affected.

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