Original article

A RETROSPECTIVE ANALYSIS OF MALIGNANT AND POTENTIALLY MALIGNANT DISORDERS DIAGNOSED IN SEVEN YEARS

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Abstract

The early diagnosis of Oral Cancer and the clinical detection of several potentially malignant lesions can be achieved by the opportunistic Screening of the Oral Mucosa of patients that search for dental assistance. The aim of this study was to perform a retrospective analysis of the origin and prevalence of malignant lesions of the oral mucosa as well as the potentially malignant disorders on patients assisted at the Stomatology and Oral Pathology Clinic of the Naval Dental Center (Odontoclínica Central da Marinha-OCM), from May 2011 to April 2018. The method used was the analysis of the clinical digital charts during this period. Independent variables were gender, age, skin, tobacco use, alcohol use; while dependent variables were the existence of malignant or potentially malignant disorders. Forty-five malignant lesions and 177 potentially malignant disorders were recorded. Among them, 25 malignant lesions and 136 potentially malignant disorders were diagnosed at the OCM. This study showed the importance of active search for lesions of oral cavity and the detection of several lesions of oral cavity by the diverse areas in Dentistry.

Keywords: *Diagnosis. Oral Cancer. Precancerous Condition. Leukoplakia. Screening.*

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INTRODUCTION

Noncommunicable diseases (NCDs) are known for being the main responsible for disease and death of the population worldwide, especially for cardiovascular disease (48% of NCDs) and cancer (21%), according to the estimative for the 2018-2019 biennium of the National Cancer Institute of Brazil (INCA) (1). It is estimated that 600,000 new cases of cancer occur each year in Brazil, including 11,200 new cases of oral cavity cancer for males and 3,500 for females. These values correspond to an estimated risk of 10.86 new cases of oral cavity cancer per 100,000 men, being the fifth most frequent in this gender, and 3.28 per 100,000 women, being the 12th most frequent among all malignant tumors. Among all oral cavity cancers, over 90% are squamous cell carcinomas (SCC), which is also the major cause of malignant tumors in the head and neck region (2-4).

Most cases of SCC affect males, over 40 years of age, long-term smokers and / or alcoholics, with low educational level and have advanced clinical stage at the time of diagnosis (5). Despite advances in diagnostic and treatment methods, the 5-year survival rate associated with SCC has remained unchanged over the past 30 years, ranging from 43% to 64%, as most cases of cancer are diagnosed in advanced stages of the disease. Thus, oral cancer is considered a public health problem (6,7). The disease may present clinically as asymptomatic even in cases with invasive lesions. Despite the relatively low incidence, morbidity and mortality is high (8,9).

Oral cancer patients diagnosed in their early stages have a greater chance of cure and survival (up to 90%) and lower morbidity than those diagnosed in advanced stages of the disease (10,11). Early detection and earlier initiation of treatment may improve mortality rates and quality of life (12). In addition, the costs of treatment increase if the disease is diagnosed at later stages, which reduces the patient's chance of cure.

Alcoholism, smoking, and possibly Human Papilloma Virus (HPV) infections, mainly by types 16 and 18, are the main risk factors for this group of tumors. According to the American Cancer Society, for lip cancer the risk factor is exposure to ultraviolet radiation (13). Primary prevention of oral cavity SCC consists of programs and measures to combat tobacco and alcohol consumption in an integrated health promotion effort (14). The prevention for lip cancer consists on the use of lip balm, hats, and decreased exposure to sunlight at times with the highest incidence of ultraviolet rays. A secondary-level preventive strategy is screening programs, which is justified by the possibility of early detection of asymptomatic lesions and increased survival rates, thus fulfilling the criteria established by the World Health Organization (WHO) (15,16,17). Screening consists of a visual-tactile examination of the oral cavity and adjacent structures, being considered a simple, fast, easy, low cost method, and without discomfort for patients (18).

However, before the onset of oral cancer, potentially malignant disorders (PMD) may be present. Thus, early identification of these changes through screening tests would prevent their progression / transformation to an SCC. This group of lesions include erythroplakia, leukoplakia, actinic cheilitis, lichenoid lesions, lichen planus, among others (04). Likewise, benign lesions affecting the oral cavity and adjacent structures can also be detected during routine dental examinations (19,20,21).

This retrospective study aims to survey the origin and prevalence of malignant lesions and PMD of the oral cavity and adjacent structures in patients treated at the OCM Stomatology and Oral Pathology Clinic in seven years.

METHODS

This was a retrospective study based on the analysis of the digital clinical records of patients treated at the OCM Stomatology and Oral Pathology Clinic from May 2011 to April 2018. These patients were referred by the Semiology Department, where dental surgeons perform an opportunistic screening of the treated patients by them, or by the several other OCM clinics. The OCM Stomatology and Oral Pathology Clinic was established in 2011 and has the clinical records of all patients who underwent to a biopsy and/or were followed up. From the collected data, gender, age, skin color, smoking, alcoholism, origin of referral and type of diagnosis (clinical or clinical/pathological) were considered independent variables; and malignant lesions and PMD, dependent variables. The patients underwent a detailed examination following standard assessment procedures. Data were collected, recorded and stored in an electronic database.

Descriptive data analysis was performed using the Microsoft Excel program.

This research was approved by the Research Ethics Committee of the Hospital Naval Marcílio Dias, under the registration CAAE nº 11941319.7.0000.5256.

RESULTS

The study included 222 people. Of the lesions observed, there were 177 PMD: 68 (38.4%) diagnoses of actinic cheilitis, 36 of them diagnosed by clinical-pathological methods and 32 only by clinical examination; 53 (29.9%) leukoplakia; 35 (19.8%) oral lichen planus and 21 (11.9%) lichenoid lesion. Malignant lesions affected 45 patients, with SCC being the most frequent, with 73.3% (n = 33) of the cases (Table 1).

The main source of referral to the Clinic of Stomatology and Oral Pathology was mostly from the clinics of OCM (72.5%), followed by other Military Organizations (MO) of the Brazilian Navy (BN), (25.7%); and lastly, referrals from civil professionals (1.8%). This distribution is shown in Figure 1. The referral origin of patients with PMD and malignant lesions can be seen in Table 2.

PMD were more frequent in patients aged 40 years and over, with a similar distribution between the groups of 40 to 59 years (86 cases; 48.6%) and over 60 years (81 cases; 45.8%). Among PMDs, the largest difference between genders occurred in actinic cheilitis, with a higher incidence in men (4.6: 1). Lichen planus and lichenoid lesions were more frequent in women and the largest difference between genders occurred in patients over 60 years of age. PMD were more frequent in Caucasian patients (105 cases; 59.3%) and among actinic cheilitis cases, 80.9% corresponded to Caucasian patients (Table 3).

Malignant lesions (ML) were more frequent in men

Table 1 - POTENTIALLY MALIGNANT DISORDERS AND MALIGNANT LESIONS

NUMBER OF LESIONS		
POTENTIALLY MALIGNANT DISORDERS		
Actinic Cheilitis	68	38,4%
Leucoplakia	53	29,9%
Lichen Planus	35	19,8%
Lichenoid Lesion	21	11,9%
TOTAL	**177**	**100%**
MALIGNANT LESIONS		
Squamous Cell Carcinoma	33	73,3%
Salivary Gland Tumors	05	11,1%
Metastatic Tumors	07	15,6%
TOTAL	**45**	**100%**

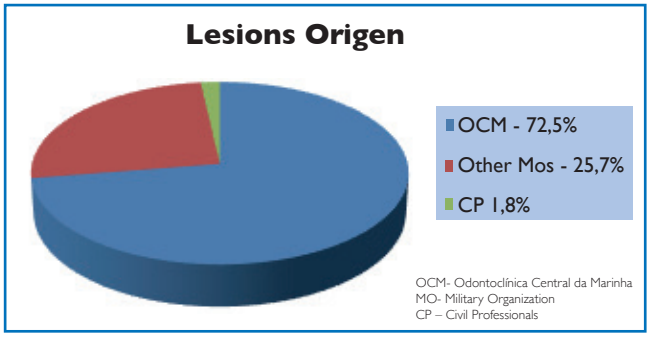

Figure 1 - Referral origen of patients

Table 2 - REFERRAL ORIGIN OF PATIENTS WITH PMD AND MALIGNANT LESIONS

Origen	DPM	ML	Total	
			n	%
OCM	136	25	161	72,5%
Other Mos	39	18	57	25,7%
CP	02	02	04	1,8%
Total	**177**	**45**	**222**	**100%**

CP: civil professionals; MOs: military organizations; OCM: Odontoclínica Central da Marinha

(57.8%), Caucasians (66.7%), aged over 60 years (66.7%), reflecting the profile of the patient with SCC. In case of metastatic tumors (MT) there was a higher incidence in women, all Caucasians, over 60 years (Table 4).

Of the 33 patients diagnosed with SCC, only 5 (15.2%) reported no smoking or alcoholism. Of the 7 patients with MT, 5 of them did not have the mentioned habits (Table 5). A relationship between the cases of SCC and smoking can be observed, because of the 33 diagnosed cases, only five patients denied smoking and alcoholism. Analyzing the habit of alcoholism, there were thirteen patients with the habit of drinking.

Table 3 - AGE, SKIN COLOR AND GENDER X POTENTIALLY MALIGNANT DISORDERS

	POTENTIALLY MALIGNANT DISORDERS								
	Actinic Cheilitis		Leucoplakia		Lichen Planus		Lichenoid Lesion		TOTAL
	M	F	M	F	M	F	M	F	
Age									
< 40 years	01		03		04			02	10 (5,6%)
40 a 59 years	30	04	12	11	07	12	07	03	86 (48,6%)
≥ 60 years	25	08	14	13	03	09	01	08	81 (45,8%)
Total	56	12	29	24	14	21	08	13	**n = 177**
Skin Color									
White	45	10	11	14	04	14	01	06	105 (59,3%)
Black	0	0	10	01	01	01	03	05	21 (11,9%)
Others	11	02	08	09	09	06	04	02	51 (28,8%)
Total	56	12	29	24	14	21	08	13	**n = 177**

Table 4 - AGE, SKIN COLOR AND GENDER X MALIGNANT LESIONS

	Squamous Cell Carcinoma		Salivary Gland Tumors		Metastatic Tumors		TOTAL
	M	F	M	F	M	F	
Age							
< 40 years	01	02	01	01		01	06 (13,3%)
40 a 59 years	05	02	01	01			09 (20,0%)
≥ 60 years	16	07		01	02	04	30 (66,7%)
Total	22	11	02	03	02	05	**n = 45**
Skin Color							
White	15	06		02	02	05	30 (66,7%)
Black	04	0	01				05 (11,1%)
Others	03	05	01	01			10 (22,2%)
Total	22	11	02	03	02	05	**n = 45**

Table 5 - POTENTIALLY MALIGNANT DISORDERS, MALIGNANT LESIONS X GENDER AND ALCOHOLISM/SMOKING

	Actinic Cheilitis		Leucoplakia		Lichen Planus		Lichenoid Lesion		Squamous Cell Carcinoma		Salivary Gland Tumors		Metastatic Tumors		TOTAL
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
Smokers	1	2	1	3		1			1	3					12
Alcoholics	26	3	4	1	3	2	1	2	3			1			46
Smokers/ Alcoh.	6		7	4	2	3	1		7	1	2				33
Smokers/ Former-alcoh.	2		1						2	1					06
Former-smkrs/ alcoholics	3	1	4	3	2	2	1		2					1	19
Former-alcoh.	2	1	2												05
Former-smkrs		1		1	1	3		1	1	1				1	10
Former-smkrs/ Former-alcoh.		1	4	1	1	1		1	4	2					15
Non-smokers/ Non-alcoholics	16	3	6	11	4	10	5	9	2	3		2	2	3	76
TOTAL	56	12	29	24	13	22	8	13	22	11	2	3	2	5	222

DISCUSSION

The vast majority of studies on oral screening practice target oral cancer and/or PMD, usually focusing on specific groups (20) and at-risk population, ie, patients over 40 years of age, alcoholics/smokers, former alcoholics/former smokers (22, 23).

The current study evaluated the prevalence of PMD and ML in the oral cavity over a period of seven years, targeting the population of military service members, the reservists from Brazilian Navy and their dependents. The screening introduced at the OCM Semiology Service is based on the current recommendation of the American Dental Association (ADA), which recommends visual-tactile examination of all individuals presenting for a dental appointment, with special attention to at-risk individuals who use tobacco, alcohol, or both. Thus, all patients are screened, regardless of risk factors, to detect not only PMD and ML, but any oral cavity lesion. According to RETHMAN et al. (18), clinicians should always be alert for signs of PMD or early-stage cancer lesions, particularly in alcoholics and smokers.

Potentially malignant disorders

The term PMD was adopted by WHO in 2005 to describe injuries and conditions associated with risk of malignant transformation (24). Its detection in patients is extremely important, since these lesions have an increased risk of developing SCC (25). Histopathological examination of these lesions may even show epithelial dysplasia (26). Most lesions are asymptomatic and the main objective in the management of these lesions is the prevention and early detection of oral cancer in its early stages (27).

Actinic cheilitis (AC) is a chronic premalignant lip keratosis caused by long exposure to solar radiation. The diagnosis of AC is based on clinical, histopathological findings and history of sun

exposure. Most lesions on the lower lip are seen in light-skinned men from the fourth to eighth decades of life, especially in those individuals who have had prolonged exposure to sunlight. More advanced cases may evolve to an SCC (4, 28, 29).

In 2004, MARKOPOULOS et al. (28) evaluated 65 patients with AC and found that all lesions were concentrated in the lower lip and occurred in light-skinned patients who were exposed to solar radiation, occurring malignant transformation in 11 of those patients (16.9%). The average age of diagnosis was 53 years old. CAMPISI and MARGIOTTA in 2001 (19) found AC in 5 patients in the evaluated sample and all patients used to work exposed to sunlight, four smoked and drank, and one was a former smoker and former drinker.

Regarding patients with AC, it is interesting to note that only 17.6% were female. The vast majority were Caucasians, having no Black people with this lesion. The non-incidence of Black patients is explained by the presence of melanin promoting a protective effect against UV radiation (4).

In the present study, among the diagnoses obtained by biopsy, there were many more cases of mild epithelial dysplasia, and few with moderate or severe dysplasia. None of the cases presented malignant transformation. Only five patients were smokers, 33 were alcoholics (four also former smokers) and six were smokers and alcoholics. Some authors consider that smoking may increase the probability of AC progressing to an SCC (3,30). However, the only etiological factor established for the development of AC and SCC remains chronic exposure to ultraviolet radiation from the sunlight (29). All patients in the sample reported a history of prolonged exposure to solar radiation and, in the case of men, the occupational issue was listed as the major cause by the patients themselves, justifying the higher incidence than in women.

Oral leukoplakia (leuko = white; plakia = spot) was defined by WHO in 1978 as "a white spot or patch that cannot be characterized clinically or pathologically as any other disease." The term is strictly clinical and does not imply in a specific tissue alteration (3). In addition, oral leukoplakia is much more common among smokers than non-smokers and its worldwide prevalence is estimated at around 2% (31). Its incidence may vary greatly, depending on the country of origin, nature of the population studied, pattern of tobacco use and criteria adopted for the definition of leukoplakia (21). In developed countries, leukoplakia lesions are found mostly in patients from middle age and may occur earlier in developing countries (21). In our study, from 53 lesions diagnosed as oral leukoplakia, only three patients were under 40 years old. Forty lesions (75.5%) occurred in patients over 50 years of age. Regarding gender distribution, prevalence was similar to both sexes.

21 out of 32 patients submitted to biopsy had a descriptive pathological diagnosis and a final diagnosis of leukoplakia through clinical and pathological correlation. Two patients had the lesions detected, but already presented previous biopsy report. Mild epithelial dysplasia was found in eight patients and moderate epithelial dysplasia in four individuals. Two biopsied cases came with a report of leukoerythroplasia with moderate epithelial dysplasia. Leukoerythroplasia is a nonhomogeneous leukoplakia with a reddish component, which almost always shows epithelial dysplasia, presenting a higher risk for malignant transformation than homogeneous leukoplakia (32). Regarding risk factors, almost half of the patients (25 cases) were former smokers and/or former drinkers, and 17 patients reported never having been a drinker or smoker. Unlike the present study, most studies show a direct cause and effect relationship between tobacco smoke and leukoplastic lesions (20,31).

For the diagnosis of lichenoid lesions, it is important to search for a specific cause such as silver amalgam mercury allergy or drug reaction, especially antihypertensive drugs.

Lichen planus (LP) is a relatively common, immunologically mediated, chronic mucocutaneous dermatological disease that often affects the oral mucosa. It is the dermatological disease that most affects the oral cavity and its prevalence affects approximately 1% of the population. The etiology is unknown, affects more middle-aged adults (30 to 60 years) and women are more affected than men by a ratio of 3:2. The literature reports that the malignant transformation potential of this lesion is less than 1%, but it exists and a large number of studies report that this malignant transformation is more common in its erosive/ulcerative and atrophic clinical forms (red forms of LP), compared to its reticular form (white). The clinical presentation of LP may vary over time and may alternate white and red phases, and patients should be properly monitored (32).

Regarding the potential of malignant transformation of lichenoid lesions (LL), it is also less than 1% in most studies, and may also alternate clinical phases such as LP. Studies do not relate LP and LL with alcoholism or smoking, and there is no apparent relationship between these injuries and these factors (24, 27, 33).

In the present study, 60% of LP and 61.9% of LL

were found in female patients, interestingly, virtually the same 3:2 ratio between genders in both lesions. The results confirmed this proportion as shown by most studies on LP. Some studies indicate a much higher incidence in females than in males (3,4).

The age of the patients with LP varied. Most of the affected patients were in middle age, between 40 and 60 years old (54.3%). Regarding lichenoid lesions, 47.6% were in this age group. Lichenoid lesions in the present study were more frequent in patients older than those diagnosed with LP.

Malignant lesions

The most prevalent malignant lesion was SCC (n = 33; 73.3%), which agrees with the literature (3,9). Seven cases represented metastatic tumors and five cases were malignant salivary gland tumors.

Most malignant lesions (SCC and metastatic tumors) were found to affect patients from the sixth decade of life. The same feature is not observed in cases of salivary gland tumors, which occurred between the fourth and seventh decades of life.

Some studies have shown a clear relationship between the intensity and duration of tobacco smoke and the risk of developing oral cancer (34). Others have shown a relationship between oral cancer and alcohol consumption (35). HASHIBE et al. in 2009 (36) demonstrated that the risk increases in patients who use cigarettes and alcohol simultaneously. CAMPISI and MARGIOTTA (2001) (19), in a screening study of 118 male individuals at risk for oral SCC, identified the presence of 1 case in a smoker and alcoholic patient. CAMPISI et al. in 2012 (8) also found a strong association between SCC lesions and male patients, smokers and alcoholics.

Finally, regarding gender, SCC lesions affected men and women in a 2:1 ratio. This proportion does not hold in relation to the habit of smoking and alcoholism. In the case of MT, there was a predominance in women.

CONCLUSION

This retrospective study revealed that more than 150 PMD and malignant lesions of oral cavity were diagnosed in the OCM over a seven-year period. In addition, it showed the importance of active search and detection of various oral cavity lesions by various specialists. Opportunistic screening is a simple technique to perform and is important both for routine screening and throughout the treatment of these patients.

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Conflicts of Interest

The authors have no conflicts or competing financial interests to declare.

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