Clinical and histopathological study of actinic cheilitis

Estudo clínico e histopatológico das queilites actínicas

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Resumo

Introdução: A queilite actínica é uma condição de natureza inflamatória que acomete o lábio inferior, e é causada pela exposição prolongada e crônica dos lábios à radiação ultravioleta proveniente dos raios solares. Objetivo: Identificar as características clínicas e histopatológicas em uma série de 40 casos diagnosticados histopatologicamente como queilite actínica. Além disso, investigar possíveis associações entre estes aspectos. Método: Caracterizado como um estudo observacional, transversal, retrospectivo e descritivo. Foram registrados dados a respeito da idade, gênero, ocupação, sintomatologia, histórico de exposição ao sol, uso de proteção solar, tabagismo, cor da pele, aspecto clínico e classificação histopatológica. Os dados foram submetidos ao teste de Qui-Quadrado de Pearson (p<0,05). Resultado: Houve uma prevalência do gênero masculino, leucodermas, com faixa etária entre 50 e 60 anos e a ocupação mais presente foi a de agricultor. Da amostra, 85% apresentou histórico de exposição crônica ao sol, em que 50% relatou uso de algum tipo de proteção solar e apenas 25% era tabagista. A principal apresentação clínica foi leucoplasia não ulcerada, e no estudo histopatológico as hiperkeratoses foram as mais presentes. Não foi possível correlacionar o grau de alteração tecidual verificada no diagnóstico histopatológico com as variáveis clínicas estudadas (p=0,112). Conclusão: Não foi possível correlacionar o grau de alteração tecidual verificada no diagnóstico histopatológico com os aspectos clínicos observados. O aspecto clínico da lesão pode mascarar alterações teciduais em diversos estágios, o que enaltece a importância do diagnóstico precoce.

Descritores: Queilite; patologia clínica; lesões pré-neoplásicas.

Abstract

Introduction: Actinic cheilitis is an inflammatory condition affecting mainly the lower lip and it is caused by chronic and excessive exposure of the lips to the ultraviolet radiation in sunlight. Objective: Identifying clinical and histopathological characteristics in 40 cases histopathologically diagnosed as actinic cheilitis. In addition, to investigate possible associations between these aspects. Method: Defined as an observational, transversal, retrospective and descriptive study, it registered data regarding age, gender, occupation, symptomatology, records of sun exposure, frequency of sunblock use, tabagism, skin color, clinical aspect and histopathological classification. The data was submitted to the chi square test of Pearson (p<0.05). Result: There was a predominance of male gender, leucoderma, and ages ranging between 50 and 60 years. The most common occupation was farming. From our sample, 85% had history of chronic sun exposure, in which 50% reported the use of some type of sunblock and only 25% were smokers. The main clinical condition was non-ulcerated leukoplakia and in the histopathological study, the hyperkeratosis were more common. A correlation between the degree of tissue alteration verified in the
Clinical and histopathological study... histopathological diagnosis and the studied clinical variables was not established ($p=0.112$).

**Conclusion:** The clinical aspect of the wound can conceal tissue alterations in different stages, emphasizing the importance of a premature diagnosis.

**Descriptors:** Cheilitis; clinical pathology; precancerous conditions.

**INTRODUCTION**

Actinic cheilitis (AC) is an inflammatory, potentially malignant condition. It affects mainly the lower lip and is caused by long-term, chronic sun exposure$^{1,2}$.

AC affects mainly fair-skinned men, over 30 years of age, with chronic sun exposure$^{1,3}$. The lesions are usually asymptomatic, and may be leukoplakia, erythroplakia or erythroleukoplakia, with or without the presence of ulcers$^2$. These lesions may be clinically characterized as acute or chronic. Acute lesions are characterized by erythematous lips, swelling, formation of blisters followed by crusts. Regression of the lesion occurs when the etiologic agent is interrupted. Chronic AC is clinically characterized by atrophy of the red lower part of the lip, with loss of elasticity and the presence of rough, scaly, keratotic plaques, unevenly overlapping the erythematous areas. In addition, the presence of ulcers and fissures is common$^{3-5}$.

Considering the well-established association between AC and the development of squamous cell carcinoma in the lower lip (SCC), biopsy of the lesion is indicated to improve the diagnostic accuracy of this lesion$^{3,4,6}$. Histopathologically, tissue changes can range from mild to severe in the epithelial and conjunctive components. In the epithelial tissue, the changes include thickening of the epithelium and the keratinized layer, ulcers, acanthosis and dysplasias that can range from mild to severe. The connective component can present solar elastosis, vasodilation and a mononuclear inflammatory infiltrate ranging from moderate to intense$^{1,6-9}$. Based on the current knowledge of AC and its potential to become malignant, early diagnosis and follow-up of the lesions is extremely important. Thus, the present study aimed to identify and associate the clinical and histopathological characteristics in a series of cases, in order to obtain subsidies for better diagnosis and to establish the prognosis of the lesions.

**METHOD**

The present study was characterized as an observational, cross-sectional descriptive study, based on retrospective data. All the cases of patients diagnosed with actinic cheilitis, through a clinical and histopathological exam, who were treated at the *Liga Interdisciplinar de Combate ao Câncer Oral* (Interdisciplinary League Against Oral Cancer) clinic of the State University of Paraíba, from October 2008 to August 2012, were evaluated (approval number 0002.0.133.000-09).

The sample was composed of 40 cases, with data on gender, age, skin color, occupation, smoking, sun exposure, painful symptoms and the clinical aspects of the lesions. To evaluate the histopathological data, a single, previously calibrated examiner, using light microscopy (Leica DM 500, Leica Microsystems Vertrieb GmbH, Wetzlar), assessed the specimens with clinical diagnosis compatible with AC. The lesion was classified as hyperkeratosis, mild, moderate or severe dysplasia or carcinoma *in situ*, according to the criteria for diagnosis of dysplasia described by Cavalcante et al.$^8$.

The results were submitted to descriptive and inferential statistical analysis using the Statistical Package for the Social Sciences (version 17.0, IBM SPSS Inc., Armonk, NY, USA) applying Pearson’s Chi-square hypothesis tests. All tests were conducted at a significance level of 5% ($p < 0.05$).
RESULT

Sample Characterization

Table 1 shows the data obtained from the analysis of the clinical characteristics of the sample submitted. It can be observed that 82.5% of the patients were male, 75% were leucodermic, 37.5% were farmers, and only 25% were smokers. The mean age was 54.5 years, with a standard deviation of ±15.75 years and 85% of the sample reported chronic sun exposure and 50% reported using sunscreen.

| Individual Characteristics | N   | %   |
|----------------------------|-----|-----|
| **Sex**                    |     |     |
| Male                       | 33  | 82.5|
| Female                     | 7   | 17.5|
| Total                      | 40  | 100 |
| **Skin color**             |     |     |
| Leukoderm                  | 30  | 75  |
| Pheoderm                   | 10  | 25  |
| Total                      | 40  | 100 |
| **Occupation**             |     |     |
| Farmer                     | 15  | 37.5|
| Driver                     | 5   | 12.5|
| Electrician                | 2   | 5   |
| Construction worker        | 3   | 7.5 |
| Fisherman                  | 1   | 2.5 |
| Tire repair man            | 1   | 2.5 |
| Student                    | 1   | 2.5 |
| Retiree                    | 6   | 15  |
| Other                      | 6   | 15  |
| Total                      | 40  | 100 |
| **Smoking**                |     |     |
| Yes                        | 10  | 25  |
| No                         | 30  | 75  |
| Total                      | 40  | 100 |
| **Sun exposure**           |     |     |
| Yes                        | 34  | 85  |
| No                         | 6   | 15  |
| Total                      | 40  | 100 |
| **Sun protection**         |     |     |
| Yes                        | 20  | 50  |
| No                         | 20  | 50  |
| Total                      | 40  | 100 |

Clinical Analysis

Upon clinical examination, the lesions studied presented aspects of leukoplakia, erythroplakia and mixed aspect. They were symptomatic in 32.5% of the sample, as shown in Table 2. All cases affected the lower lip. Other features such as blurred demarcation of the vermilion border of the lip, erythema, atrophy, keratosis, erosion, crusts and fissures were observed.
Table 2. Sample distribution by clinical and pathological features

| Characteristic                     | n  | %   |
|------------------------------------|----|-----|
| Painful symptomatology             |    |     |
| Yes                                | 13 | 32.5|
| No                                 | 27 | 67.5|
| Total                              | 40 | 100 |
| Clinical aspect of the lesion       |    |     |
| No-ulcerated leukoplakia           | 19 | 47.5|
| No-ulcerated Erythroplakia         | 10 | 25  |
| Erosion/ulceration                 | 1  | 2.5 |
| Mixed aspects                      | 10 | 25  |
| Total                              | 40 | 100 |
| Histopathological Diagnosis        |    |     |
| Hyperkeratosis                     | 20 | 50  |
| Mild Dysplasia                     | 8  | 20  |
| Moderate Dysplasia                 | 10 | 25  |
| Severe Dysplasia                   | 2  | 5   |
| Total                              | 40 | 100 |

Histopathological Analysis

Typical characteristics of this type of lesion such as hyperplasia of the epithelial layer of the vermilion of the lip, disorderly maturation, cellular atypia, varying degrees of mitotic activity and hyper-keratinization were observed. Basophilic degeneration of the collagen fibers in the connective tissue (solar elastosis), common in AC, was also observed, as well as the presence of predominantly mononuclear inflammatory infiltrate.

The sample was classified according to the histopathological diagnosis as hyperkeratosis, mild, moderate and severe dysplasia, as shown in Table 2. The no-ulcerated aspect of leukoplakia was present in 10 cases of hyperkeratosis, while no-ulcerated erythroplakia and mixed aspects were present in five cases each, displaying equal frequency of mild dysplasia. Moderate dysplasia was present in five lesions with the clinical aspect of no-ulcerated leukoplakia. Only one lesion with mixed clinical aspect and one with erosion/ulceration were histopathologically classified as severe dysplasia. It was not possible to establish a statistically significant correlation between the clinical aspect and the histopathological classification of the ACs (p = 0.112) (Table 3).

Table 3. Correlation between clinical aspects and histopathological classification in number of cases

| CLINICAL ASPECT            | HISTOPATHOLOGICAL CLASSIFICATION |
|----------------------------|---------------------------------|
|                            | Hyperkeratosis | Mild dysplasia | Moderate dysplasia | Severe dysplasia |
| No-ulcerated leukoplakia   | 10 (52.6%)     | 4 (21%)        | 5 (26.3%)          | -                |
| No-ulcerated Erythroplakia| 5 (50%)        | 2 (20%)        | 2 (20%)            | 1 (10%)          |
| Mixed aspect               | 5 (50%)        | 2 (20%)        | 3 (30%)            | -                |
| Erosion/ulceration         | -               | -              | -                   | 1 (100%)         |

DISCUSSION

Leukoplakia, erythroplakia, oral lichen planus and AC are the oral lesions with the greatest potential for becoming malignant. AC is considered a potentially malignant disorder, characterized by a variety of clinical aspects that may not correspond with its real severity.
The primary etiological agent is chronic exposure to solar radiation. The malignant transformation can occur, causing SCC, which develops slowly and causes late metastasis.

AC predominantly affects men and is more common in individuals with fair skin. In the present study, the data align with the literature, since leucoderma males composed most of the sample. According to previous studies, individuals over 50 years of age are the most affected, reinforcing the finding of cumulative damage coming from solar radiation. However, Souza Lucena et al. observed that fair-skinned men, average age of 37 years, were the most affected by AC. According to these authors, this association can be justified by the prevalence of men in activities involving chronic exposure to the sun, in addition to lack of self-care which can result in more lesions.

Therefore, the occupational issue is closely related to the lesion. This can be associated with the fact that workers who are chronically exposed to the sun are more affected, especially farmers, fishermen, couriers and traffic cops. Corroborating previous studies, most of the sample of the present study was composed of farmers with a history of chronic sun exposure.

In relation to location, the literature shows that the lower lip is the most affected area, due to greater exposure to direct solar radiation. For the present study, all specimens were removed from the lower lip for biopsy, corroborating the relevant literature.

The appearance of potentially malignant oral lesions, such as AC, have been related to exposure to risk factors such as smoking, alcohol and excessive sun exposure. In this context, smoking, like alcohol, can be a confounding variable since it facilitates the appearance of leukoplakias which have a differential diagnosis from AC. Thus, for such cases, it is important that patients report their history of chronic exposure to the sun. There is controversy in the literature regarding the association of smoking with the development of AC. While Souza Lucena et al. observed that only 18.9% of patients with AC were smokers, Markopoulos et al. reported that 60% of individuals with AC were smokers. The data used in the present study showed that 25% of patients with AC were smokers.

Among the main clinical characteristics, AC can be characterized by the presence of eukoplakia and ulcerated lesions and lip dryness. For Piñera-Marques et al., the main clinical alterations of AC are erythema, keratosis, atrophy, erosion and fissures. However, in the present study, an increased frequency of no-ulcerated leukoplakia aspects was observed. According to Gonzaga et al., there is no correlation between the clinical appearance and the degree of histopathological damage, as there are no specific clinical aspects to distinguish AC from CSS, which enhances the importance of histopathological analysis.

The histopathological aspects of AC can range from hyperkeratosis to epithelial dysplasia. Dysplastic changes can occur in the deeper layers of the epithelium. The existence of epithelial dysplasia, even if mild, indicates increased risk and subsequent development of cancer. At the level of the epithelium, the first microscopic changes are hyperkeratosis, in addition to atrophy or epithelial hyperplasia. At a more advanced stage, these findings are amplified and the thorny layer becomes thicker. Keratin pearls, as well as areas of cellular atypia, can also be found. In the connective tissue, some important changes such as the basophilic degeneration of collagen fibers, known as solar elastosis, can also be observed. In this change, it has been ascertained that the elastic and collagen fibers are replaced by a granular, basophilic, amorphous and acellular material that usually contains dilated blood vessels. An inflammatory infiltrate, ranging from moderate to intense, can be observed.

In the present study, hyperkeratosis was the histopathological aspect most commonly observed, followed by moderate, mild and severe epithelial dysplasia. The greatest frequency of hyperkeratosis was seen in lesions with no-ulcerated leukoplakia aspect, despite having also been the most observed histopathological classification in lesions with mixed and no-ulcerated erythroplakia aspect. Moderate epithelial dysplasias were also commonly seen in lesions clinically classified as no-ulcerated leukoplakia. Only two lesions were histopathologically
classified as severe dysplasia, having been observed specifically in lesions with no-ulcerated erythroplakia and erosion/ulceration aspect. Therefore, it was not possible to establish a correlation between the clinical characterization and histopathological classification of the lesions in the studied sample.

CONCLUSION

It was not possible to correlate the degree of tissue change found in the histopathological diagnostic with the clinical aspects observed. Thus, it can be concluded that the clinical aspect of the lesion can mask tissue changes at various stages, including the most advanced and of greatest risk to the patient. This fact highlights the importance of early diagnosis. Therefore, it is imperative that the dental surgeon have knowledge of CA in order to be able to make a correct diagnosis and detect the clinically visible changes in the lip epithelium in the initial stages.

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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