http://dx.doi.org/10.1590/1981-86372022003020200232

Lip carcinoma mimicking keratoacanthoma: case reports

Carcinoma de lábio mimetizando queratoacantoma: relato de casos

Luciano Henrique Ferreira **LIMA**[1] 0000-0003-0118-0958

Ana Paula Cota **VIANA**[2] 0000-0002-5648-8565

Giovanna Ribeiro **SOUTO**[2] 0000-0003-3617-8794

Soraya de Mattos Camargo **GROSSMANN**[2] 0000-0002-8920-3853

Carlos Roberto **MARTINS**[2] 0000-0002-5097-8504

Hermínia Marques **CAPISTRANO**[2] 0000-0001-8546-0118

ABSTRACT

Oral squamous cell carcinoma presents more than 90% of oral cancers and the subtype lip squamous cell carcinoma comprise 25% to 30%. This subtype may have a clinical appearance similar to keratoacanthoma, which hinders the appropriate diagnosis between these conditions, but an adequate diagnosis and differentiation between these lesions is necessary, since the clinical course between them is different, the first being more invasive. Chronic exposure to ultraviolet radiation is the most important etiology associated with the development of this condition. The aim of this study is to describe three cases of lip squamous cell carcinoma with emphasis on clinical and histological characteristics that mimic keratoacanthoma. Although this carcinoma of the lip often occurs in a location that is easy for patients and health professionals to view, in most cases the diagnosis of the disease is delayed, resulting in aesthetic deformations due to more aggressive treatment.

Indexing terms: Carcinoma, squamous cell. Diagnosis, differential. Lip.

RESUMO

Carcinoma de células escamosas oral representa mais de 90% dos cânceres orais e o subtipo carcinoma de células escamosas de lábio compreende 25% a 30% de todos os cânceres orais. Este subtipo pode ter uma aparência clínica semelhante ao queratoacantoma, o que dificulta o adequado diagnóstico entre estas condições, mas se faz necessário o adequado diagnóstico e diferenciação entre estas lesões, já que o curso clínico entre elas é diferente, sendo o primeiro mais invasivo. A exposição crônica à radiação ultravioleta é o fator causal mais importante associada ao desenvolvimento desta condição. O objetivo desse estudo é descrever três casos de carcinoma de células escamosas de lábio com ênfase nas características clínicas e histológicas que imitam o queratoacantoma. Embora o carcinoma

[1] Universidade Estadual de Campinas, Faculdade de Odontologia de Piracicaba, Departamento de Diagnóstico Oral. Av. Limeira, 901, 13414-903, Piracicaba, SP, Brasil. Correspondence to: LHF LIMA. E-mail: <luclima96@hotmail.com>

[2] Pontifícia Universidade Católica de Minas Gerais, Departamento de Odontologia. Belo Horizonte, MG, Brasil.

How to cite this article

Lima LHF, Viana APC, Souto GR, Grossmant SMC, Martins CR, Capistrano HM. Lip carcinoma mimicking keratoacanthoma: Case reports. RGO, Rev Gaúch Odontol. 2022;70:e20220030. http://dx.doi.org/10.1590/1981-86372022003020200232

de células escamosas de lábio frequentemente ocorra em local de fácil visualização pelos próprios pacientes e profissionais de saúde, na maioria dos casos o diagnóstico é tardio, resultando em deformações estéticas devido ao tratamento mais agressivo.

Termos de indexação: *Carcinoma de células escamosas. Diagnóstico diferencial. Lábio.*

INTRODUCTION

Squamous cell carcinoma of the head and neck region is the sixth most common type of cancer in the world, being characterized by a group of highly biologically diversified tumors [1]. In the present context, oral squamous cell carcinoma is responsible for more than 90% of oral cancers [2]. The lip squamous cell carcinoma (LSCC) comprises 10% of all cancers of the head and neck region and can be preceded by actinic cheilitis, a potentially malignant disorder [2,3].

The most important etiological factor associated with the development of LSCC is the chronic exposure to ultraviolet radiation [2]. The alcohol and tobacco abuse also play a synergistic role as risk factors for this pathology. The lower lip is most frequently involved, with predilection for male patients with 50 years old or older, and a mean age of 65 years. The treatment of choice for LSCC is complete surgical excision [3,4].

One of the most important differential clinical diagnosis of the LSCC is the keratoacanthoma. The latter is a benign, self-limiting proliferative epithelial lesion that affects the vermilion border of the lips. The clinical and histopathological characteristics of keratoacanthoma may resemble those of a well-differentiated squamous cell carcinoma [4-6]. The spontaneous regression of the keratoacanthoma is weakly reported because the characteristics, both clinical and histopathological, are similar between keratoacanthomas and well-differentiated LSCC, which commonly represents a diagnostic challenge between these lesions [5].

Due to both injuries are often found on the lower lip, dental surgeons may be the first health professionals to diagnose the keratoacanthoma or LSCC. Therefore, they must be aware of its possible presence of both lesions and have knowledge for its inclusion as a diagnostic hypothesis [5-7].

The aim of this study is to report three clinical cases with definitive diagnosis of LSCC that presented clinical characteristics similar to keratoacanthoma.

CASE REPORT

Case 1 – A 50-year-old man, leukoderma, farmer, was referred to the Department of Dentistry of the Pontifical Catholic University of Minas Gerais for the diagnosis and treatment of a lesion in the mouth, with approximately two years of evolution. The patient reported that the lesion started as a small area with fissures and ulcers, presenting regression and growth episodes. About the habits, he is smoker and alcoholic for 30 years and remains for long-term exposure daily to ultraviolet radiation, due to rural work. His medical history was irrelevant, without systemic disease or daily use of medications. On extraoral examination, an exophytic, painless, proliferative lesion, with a firm consistency, with an irregular appearance, with erythematous areas at the base, covered with a brownish crust in the central region of the vermillion of the lower lip was observed. The lesion measured 35 mm in its largest diameter (figures 1A and B).

No changed lymph nodes were detected on palpation. In the intraoral examination, was observed total upper and lower edentulism, in addition to a hyperplastic lesion in the lower right alveolar crest associated with the removable prosthesis. The clinical diagnosis hypotheses for the lesion in the lower lip were squamous cell carcinoma of the lip (LSCC), keratoacanthoma and cutaneous horn. The patient was underwent incisional biopsy, under local anesthesia, and the specimen was sent to the Oral Pathology Service for anatomopathological diagnosis (figure 1C). Histological sections, stained with hematoxylin and eosin (HE), showing an invasive proliferation of malignant squamous epithelial cells in the stroma, forming islands (figure 2A) with eosinophilic cytoplasm, hyperchromatic nuclei and increased proportion of nuclei-cytoplasm, cellular and nuclear pleomorphism, atypical mitosis, keratin pearls in the lesional epithelium and cells with individual keratinization (figure 2B and C). The anatomopathological diagnosis was squamous cell carcinoma. The

patient was referred to an Oncology Service and the recommended treatment was surgical excision with a safety margin (figure 1D).

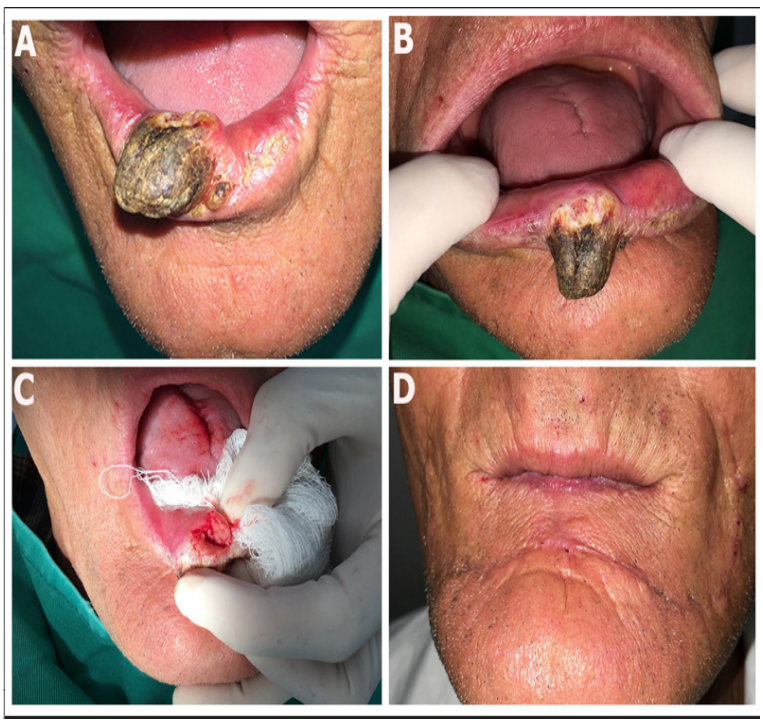

Figure 1 – A) Clinical view showing exophytic lesion in the lower lip vermelion B) Extension of the lesion for lip mucosa. C) After the incisional biopsy. D) Six months after surgery.

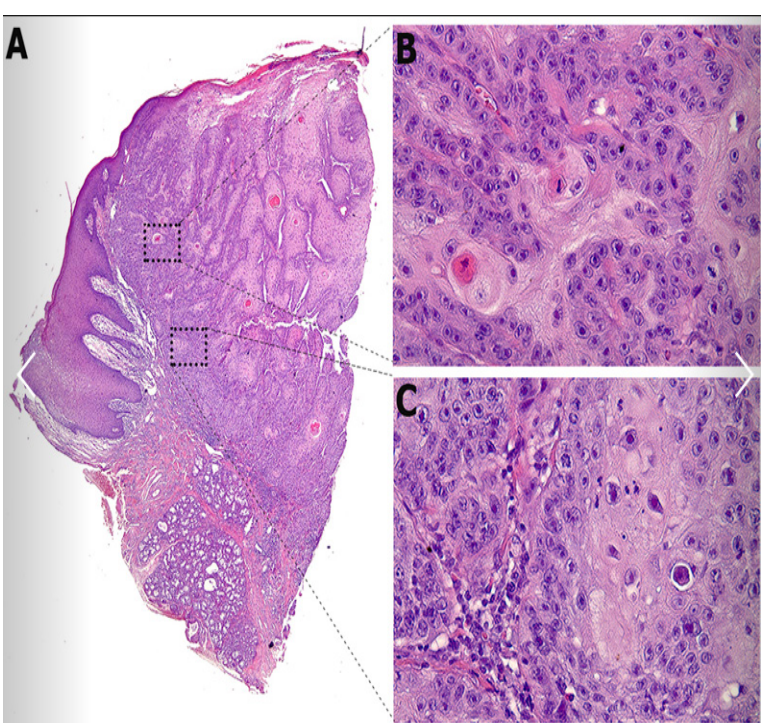

Figure 2 – A) Histological aspect of the mucosa covered by stratified paraceratinized squamous epithelium, with the invasion of malignant epithelial cells in the connective tissue with a solid growth pattern. B) and C) Amplified view showing pleomorphism, hyperchromatic nuclei, atypical mitosis and dyskeratosis.

Case 2 – A 58-year-old man, feoderma, was referred to the Department of Dentistry of the Pontifical Catholic University of Minas Gerais for diagnosis and treatment of a lesion on his lower lip, with evolution of about one month. The patient reported that the lesion started as a "small ball" that ulcerated, but was asymptomatic. He denied smoking and drinking habits, without chronic exposure historic to ultraviolet radiation. His medical history was irrelevant, without systemic disease or daily use of medications. On extra-oral examination, he presented a nodular lesion with slightly raised edges, firm consistency, localized in the right lateral region of the lip vermillion, close to the labial commissure. The lesion measured about 8 mm in its largest diameter (figure 3A). No changed lymph nodes were detected on palpation. In the intraoral examination, erythematous lesions were observed on the hard palate associated with the use of removable prosthesis. The clinical diagnosis hypotheses for the lip lesion included squamous papilloma, keratoacanthoma and squamous cell carcinoma. An incisional biopsy was performed and the specimen was sent to the Oral Pathology Service. The histological sections, stained with hematoxylin and eosin, presented an invasive proliferation of islands and strands of malignant squamous epithelial cells with hyperchromatic nuclei, increased relation in nucleus-cytoplasm, cellular and nuclear pleomorphism, increased quantity of mitosis and atypical mitosis. The anatomopathological diagnosis was squamous cell carcinoma. The patient was referred to an Oncology Service and the preconized treatment was a surgical excision.

Case 3 – A 65-year-old woman, feoderma, was referred to the Department of Dentistry of the Pontifical Catholic University of Minas Gerais for diagnosis and treatment of a lesion on the lower lip, with about three years of evolution. In the anamnesis, she reported that the lesion started out as a small ulcer and showed progressive growth. She reported smoker habit for 20 years and occasional exposure to ultraviolet radiation. Her medical history was irrelevant, without systemic disease or daily use of medications. On extraoral examination, an exophytic lesion, irregular, with a firm consistency, covered by a crust, localized in the left lateral region of the vermilion of the lower lip was observed. The lesion measured about 16 mm in its largest diameter (figure 3B). No changed lymph nodes were detected on palpation. On intraoral examination, there were no significant changes. Diagnostic clinical hypotheses included squamous cell carcinoma and keratoacanthoma. The patient was underwent an incisional biopsy and the specimen was sent to the Oral Pathology Service. The histological sections, stained in hematoxylin and eosin, presented a crateriform lesion filled with keratin. The surface epithelium exhibited invasive proliferation of islands and strands of malignant squamous cells in the subjacent stroma with hyperchromatic nuclei, increased relation in nucleus-cytoplasm, increased quantity of mitosis, atypical mitosis, numerous dyskeratosis and keratin pearls in the lesional epithelium, with the presence of individual cell keratinization. Histopathological diagnosis was squamous cell carcinoma. The patient was referred to an Oncology Service and the treatment was surgical excision of the lesion.

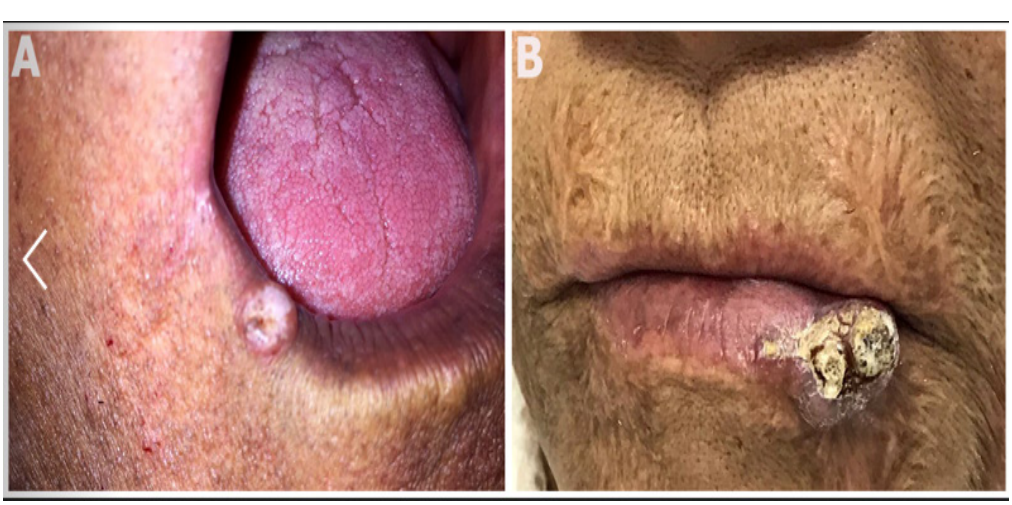

Figure 3 – A) Exophytic lesion in the lateral of the lip vermelion in the case 2. B) Exophytic lesion in the lateral of the lip vermelion in the case 3.

DISCUSSION

LSCC is a common malignant tumor, representing 25% to 30% of all oral cancers [8]. In a retrospective study in the Brazilian population, this subtype was the most prevalent in older men with the man-woman ration of 5:1, with a significant association between chronic sun exposure in the workplace and the incidence of squamous cell carcinoma in the lower lip, being this anatomical region most exposed to the sun exposure than the upper lip [2]. Outdoor work is more common for men, making them more subject to sun exposure, which probably explains the male predominance of this type of cancer. In addition, leukoderma people tend to be more susceptible to this cancer [4]. The three patients described in this study, who developed the squamous cell carcinoma on the lower lip, were aged between 50 and 65 years, but only one of them had chronic exposure historic to the sun and was leukoderma.

Due to several factors and characteristics that can be similar, the correct diagnostic differentiation between the LSCC and keratoacanthoma can represent, in many cases, a challenge. Leukoderma people with chronic habit and exposure to the ultraviolet radiation are included in the risk factors for both lesions. Both lesions have a predilection for the male gender, with age range between middle-aged adults and the elderly and localized more frequently in the lower lip. Keratoacanthoma is a self-limiting benign proliferative epithelial lesion that usually presents an initial proliferative phase, followed by a maturation phase and a involutive or stationary phase, that may or may not have spontaneous regression. In contrast, the squamous cell carcinoma, in any localization, is a malignant epithelial neoplasia that does not undergo spontaneous involution [5,9].

In the first case of this study, the lesion was observed by the patient about two years before, with a report of growth followed by an initial spontaneous regression, which started to grow later, which suggested the diagnostic hypothesis of keratoacanthoma. In the three reported cases, however, the anamnesis data, as well as the clinical characteristics of the lesions, required a clinical differential diagnosis between the LSCC and the keratoacanthoma. Through incisional biopsy followed by anatomopathological examination, the conclusive diagnosis of LSCC was established and the recommended treatment was the surgical removal of malignant neoplasms.

Vieira et al. [10] report that keratoacanthoma does not need to be removed, as it tends to regress spontaneously. However, in view of the challenge for the diagnostic differentiation between this benign lesion and the LSCC, the approach chosen in these reported cases was perform an incisional biopsy, followed by anatomopathological examination, to obtain a conclusive diagnosis and adequate management as early as possible.

Studies have been developed in search of more specific methods to adequate differentiation between keratoacanthoma and LSCC. In previous studies, differences in the expression of p53 protein [11], tumor suppressor p16 protein [12] and type 1 angiotensin receptor [13] between keratoacanthoma and squamous cell carcinoma were evaluated, but no significant differences were found that could make these markers useful for this differentiation.

The histological analysis of the keratoacanthoma show some explicit characteristics The superficial epithelium on the lateral edges of the lesion does not change, but in the central area it is possible to visualize a defined acute angle between the lesion and this lining epithelium, forming a crateriform depression filled with keratin. The epithelial cells at the base of the lesion proliferate to the underlying connective tissue, inducing a dense chronic inflammatory response. Dyskeratosis may be present, as keratin pearls or individual cell keratinization [14].

Regarding the typical histological aspects of the LSCC, the presence of islands of malignant or invasive squamous epithelial cells is observed. Tumor cells demonstrates atypical mitosis, eosinophilic vitreous cytoplasm and enlarged nuclei, often hyperchromatic, in addition to the increased nucleus-cytoplasm ratio. Varying degrees of nuclear and cellular pleomorphism are observed, as well as the presence of keratin pearls are variable. In addition, there may be keratinization in individual cells [15].

The surgical excision is the treatment of choice for LSCC, unless it is contraindicated by the patient's comorbidity. The NCCN (National Comprehensive Cancer Network) guidelines recommend the surgical removal with approximately 1 to 2 cm of margin clinically free of tumor, showing success rates of 92% and 100%. Radiotherapy should be considered as adjuvant therapy for those cases in which free margins cannot be performed and for high-risk or less differentiated

tumors [16]. The cases reported in this study followed the treatment proposed by the scientific literature, only with surgical excision associated with negative margin, and had complete resolution of this pathology. No reconstructive technique with grafts or flaps was necessary, since the surgical defects were not significant.

The overall survival for LSCC is generally 87.8% in 5 years and 63.3% in 10 years. In the absence of cervical metastasis, lip cancer has a favorable prognosis and great chances of cure [4]. The patients in this study have been followed up for more than 3 years, with no signs of recurrence or metastasis.

CONCLUSION

Due to its localization, the LSCC is easily viewed by patients and health professionals. However, the diagnosis of the disease is, in most cases, late, probably due to the initial absence of symptoms, leading the patient to postpone a professional evaluation and diagnosis of the lesion. The clinical characteristics of well-differentiated LSCC and keratoacanthoma are similar, but the clinical course of these lesions and aggressiveness are quite different.

Early diagnosis is always important for diseases and injuries, especially for malignant lesions. Late diagnosis and treatment can lead, therefore, to functional alterations and aesthetic implications that may be associated with worsening quality of life for patients with this disease.

Collaborators

LHF LIMA, participation in the clinical case, responsible for the textual redation, text formatting, traduction and adaptation to the magazine's rules. APC VIANA, participation in the clinical case and redation. GR SOUTO, conductor of the clinical cases, redation and correction. SMC GROSSMANN, conductor of the clinical cases, redation and redation. CR MARTINS, participation in the clinical case and correction. HM CAPISTRANO, conductor of the clinical case, supervision, responsible for the textual correction, traduction and adaptation to the magazine's rules.

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Received on: 29/12/2020
Final version resubmitted on: 27/2/2021
Approved on: 19/5/2021

Assistant editor: Marcelo Sperandio