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## Oral squamous cell carcinoma: General aspects and case reports

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### Abstract

**Introduction:** Of the malignant tumors of the oral cavity, 90% of them are oral squamous cell carcinomas, with a predilection to develop in the tongue and floor of the mouth being the most common sites. It is a lethal and disfiguring disease with an increase in its incidence, especially in the young population.

**Case Report:** We present the case of 2 patients of different gender, who attended a check-up due to the presence of a lesion on the right lateral edge of the tongue, with a time of 1 and 6 months of evolution; with different risk factors. When performing the inspection for the neck area, adenopathies were palpated in both patients. Incisional biopsies were performed for histopathological study through which the diagnosis of squamous cell carcinoma (OSCC) was obtained.

**Conclusion:** The timely detection of oral cancer and premalignant lesions is a vital issue for the patient's prognosis. Due to the high incidence of OSCC, the dental community is invited to detect, manage, refer and/or diagnose this pathology, for the benefit of the patient.

**Keywords:** Oral squamous cell carcinoma, cancer, metastatic, risk factors, tobacco

### Introduction

More than 90% of malignant tumors diagnosed in the oral cavity are oral squamous cell carcinomas, which are preferably located on the tongue.<sup>1</sup> It is a lethal and deforming disease that has shown an increase in its incidence, especially in young patients, and around 300,000 new cases occur each year<sup>[1, 2]</sup>.

The most common sites where oral squamous cell carcinoma (OSCC) occurs, are the tongue, the floor of the mouth, the gums, or the oral mucosa in the case of patients who chew tobacco or betel nut<sup>[3]</sup>.

### Risk Factors

Within the risk factors are mainly alcohol and tobacco in their different presentations, as well as the human papillomavirus (HPV), or associated with alterations in the genome such as xeroderma pigmentosum, aplastic anemia and dyskeratosis congenital<sup>[4]</sup>.

### OSCC Development

The development of oral cancer is a complex process that comprises multiple steps. When normal keratinocytes in the oral mucosa are chronically exposed to risk factors, homeostasis can be disrupted, and genetic instability can result.

Uncontrolled growth and proliferation generate adaptive changes in surrounding cells that promote local invasion and produce collaboration of surrounding stromal cells.

Subsequently, the cells begin to secrete factors such as MMP2 (matrix metalloproteinases 2), MMP9 (matrix metalloproteinases 9), MMP13 (matrix metalloproteinases 13), reactive oxygen species, VEGF (vascular endothelial growth factor), CXCL1, CXCL8 (chemokines [CXC motif] ligand 1 and 8), PDGF (platelet growth factor), IL-1 and IL-8 (interleukin 1 and 8),

FGF-2 (fibroblast growth factor 2), TGF- $\beta$  (transforming factor -  $\beta$ ), TNF- $\alpha$  (tumor necrosis factor  $\alpha$ ), GM-CSF (granulocyte-macrophage colony-stimulating factor).

All this microenvironment favors the loss of cell adhesion and facilitates the mesenchymal transition of the epithelium.

Vimentin and N-cadherin can be expressed in these cells. The CAF (tumor-associated fibroblast) markers are  $\alpha$ -SMA ( $\alpha$ -smooth muscle actin) and  $\alpha 6$  integrin. Endothelins may contribute to promigratory paracrine signaling between CAFs and oral cancer cells. It also promotes the proliferation and survival of CXCL1 and CXCL8 endothelial cells. Endothelial cells produce factors such as EGF, which increase migration [5].

Thus, periodontopathogenic bacteria such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum* have been shown to play a role in the development of oral cancer [6].

### Metastasis

OSCCs have the potential to produce metastases and can be of two types: regional and/or distant.

Regional metastasis occurs when tumor cells from the primary site enter the lymphatic channels to migrate to the lymph nodes.

Lymph node metastasis is a critical prognostic indicator in these cases. The most common site of OSCC metastasis is the cervical lymph nodes, and this reduces the survival rate by 50%. Cancer cells usually spread to lymph nodes on the same side as the primary site, however bilateral or contralateral node metastasis is possible, although rare.

For a tumor in a primary site to spread to a distance, it requires certain biological conditions, such as the invasion-metastatic cascade (Fig 1).

### Invasion-Metastatic Cascade

The most common site of distant metastasis of OSCC is the lung, but metastasis to other organs such as mediastinal nodes, liver, and bone can occur.

Distant metastasis worsens the prognosis and reduces the chances of successful treatment [7].

### Diagnosis

Early detection of oral cancer is important for a better treatment success rate. Therefore, it is crucial to take into account risk factors or premalignant oral cavity lesions, such as leukoplakia, erythroplasia, oral lichen planus and chronic inflammation (e.g. in the case of constant trauma).

There are complementary diagnostic methods that are not as informative as a biopsy but can help distinguish between a benign and a potentially malignant lesion, such as toluidine blue staining, light-based detection techniques (autofluorescent imaging), and future methods such as biomarkers in saliva are expected to be useful for diagnosis [8].

### Case Reports

Both patients attended the Department of Periodontics of the Faculty of Dentistry of the Autonomous University of Coahuila.

#### Case 1

A 65-year-old patient, male, denied a considerable medical history, reports a habit of smoking for 40 years, and is classified as a heavy smoker, he works in mining.

During the interrogation, the patient reports a lesion on the

tongue that produces pain, with occasional mild bleeding, with an evolution period of approximately 6-7 months, which began as a small ulcer that increased in size over time, the tissues around the site of injury are indurated from the most anterior to the posterior portion of the tongue.

The lesion has irregular, leukoedematous borders and irregularly arranged, its consistency is indurated, covering the area of the right lateral border and lower part of the tongue (Fig 2 and 3).

On clinical examination, some additional data were observed that could be involved in the formation of the lesion, such as the intimate contact of the lower incisors with sharp edges and wear (Fig 4) that coincide in shape with the ulcerated lesion.

When inspecting the neck, unilateral adenopathies (on the right side) were palpated, which were hard, immobile, and painless from the right submandibular lymph node chain.

Due to the characteristics and evolution time of the lesion, the decision was made to perform an incisional biopsy for subsequent histopathological analysis. To guide the protocol for taking the biopsy, the detection kit for oral cancer was used as a complementary diagnostic method, which consists of the following steps:

1. Apply 1% acetic acid with a cotton swab for 30 seconds to the suspected area.
2. Apply with a swab, 1% toluidine blue for 1 minute (Fig 5).
3. Reapply 1% acetic acid for 30 seconds, and instruct the patient to rinse.
4. The lesion or suspicious area is considered a positive test if it acquires a dark blue coloration in all or part of it. (Fig 6)
5. The incision should be made including healthy tissue and the toluidine blue positive area.
6. Subsequently, the specimen must be placed in a bottle with 10% formalin.
7. Perform histopathological analysis.

A spindle-shaped fragment of 1.0 x 1.0 cm is obtained, with a soft consistency and an external surface with a central ulcerated area and a whitish border (Fig 7).

### Microscopic Description

Microscopic sections reveal segments of mucosa in which a keratinized, acanthotic and hyperplastic stratified squamous epithelium is observed, from which masses and groups of cells with changes consisting of important cellular pleomorphism, nuclear hyperchromatism, enlarged nuclei, enlarged cells, abundant abnormal mitoses, and little individual keratinization. These cells invade the underlying connective tissue surrounded by a moderate lymphoplasmacytic chronic inflammatory infiltrate and moderate vascularity (Fig 8).

### Diagnosis

Moderately differentiated squamous cell carcinoma.

#### Case 2

59 years old, female patient, with a history of Diabetes mellitus with 12 years of evolution, controlled and treated with glibenclamide and metformin; social and occasional smoker, podiatrist by trade.

The patient refers pain to the manipulation of the lesion present on the tongue, with a month of evolution, the patient ignore the origin of it and reports having noticed until the

lesion manifested the present appearance. Clinical examination revealed an irregular, ulcerated lesion with whitish, indurated edges, and multiple fissures in the anterior and middle portion of the edge of the tongue, with hemorrhage on minimal manipulation (Fig 9 and 10). Indentations in the lesion that correspond to the occlusal surfaces of the lower premolars and an upper removable prosthesis with poor adaptation and generalized periodontal disease are also observed (Fig 11).

When inspecting the neck area, ipsilateral, hard, immobile, and slightly painful lymphadenopathies of the right submandibular lymph node chain and the superficial cervical chain were palpated (Fig 12).

The same protocol for staining the lesion is performed and an incisional biopsy of an anterior and a posterior fragment is performed based on the stained areas (Fig 13).

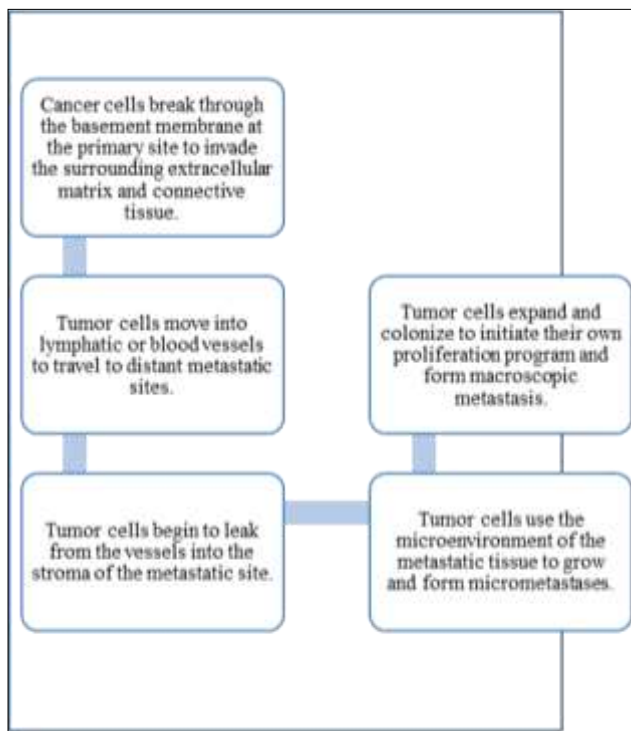
An anterior spindle-shaped fragment of 1.0 x 1.0 cm is obtained, and another posterior one of 0.8 x 0.8 cm, both soft and with a granular external surface (Fig 14).



**Fig 3:** Lateral view of the lesión on the dorsum of the tongue



**Fig 4:** Lower incisors with crowding



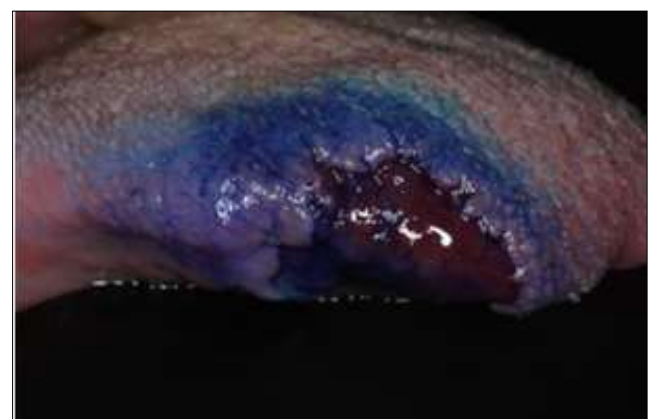
**Fig 1:** Metastatic invasión cascade diagram



**Fig 5:** Positive test with dark blue staining

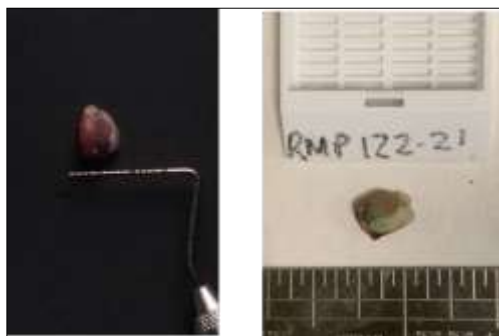


**Fig 2:** Front view of the lesión on the dorsum of the tongue

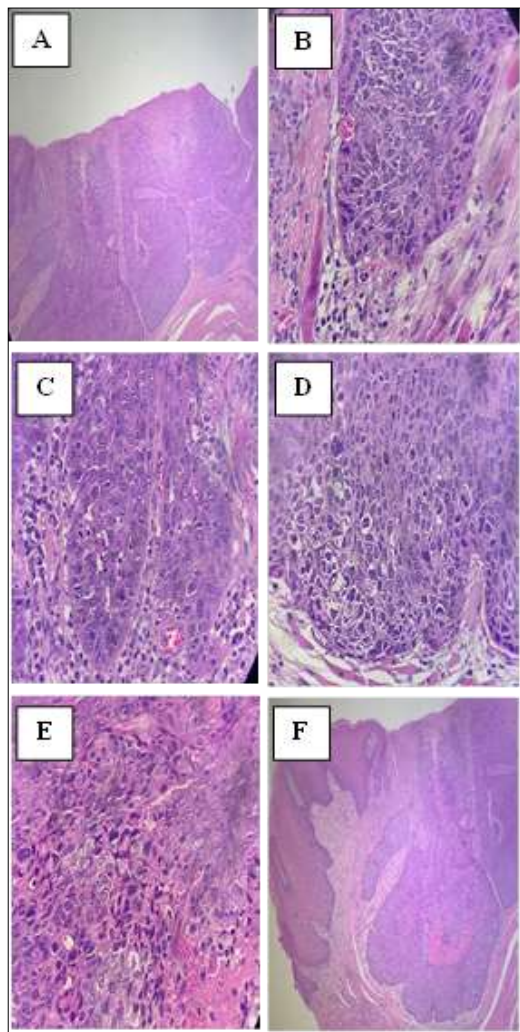


**Fig 6:** Toluidine blue staining





**Fig 7:** Fragment obtained in a spindle-shaped



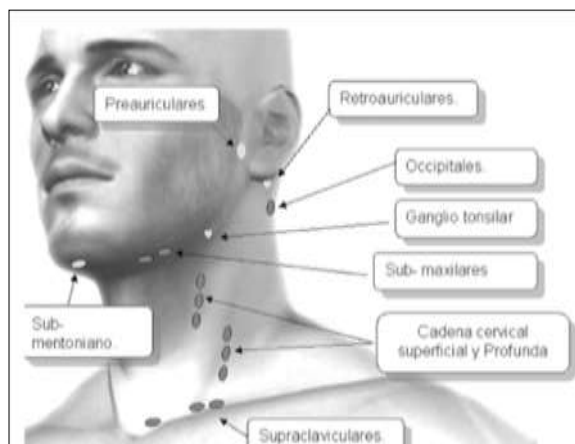
**Fig 8:** Microscope sections



**Fig 10:** View of the lesión from the ventral aspect of the tongue



**Fig 11:** Right lateral photograph with the prosthesis in place



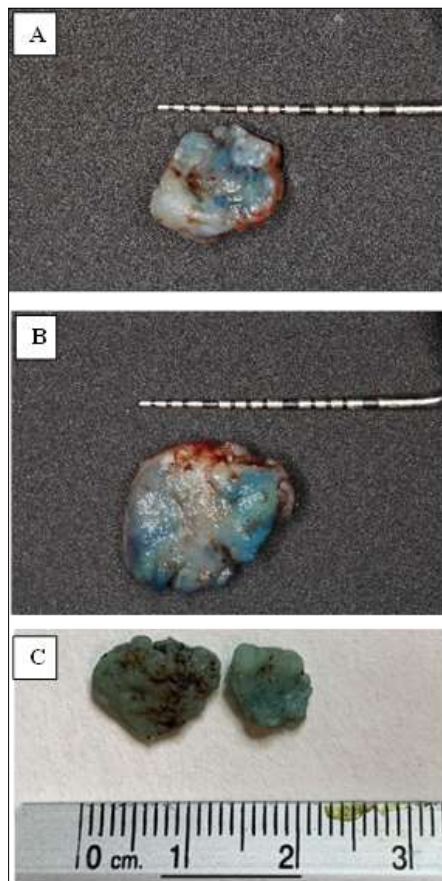
**Fig 12:** Ganglionic chains



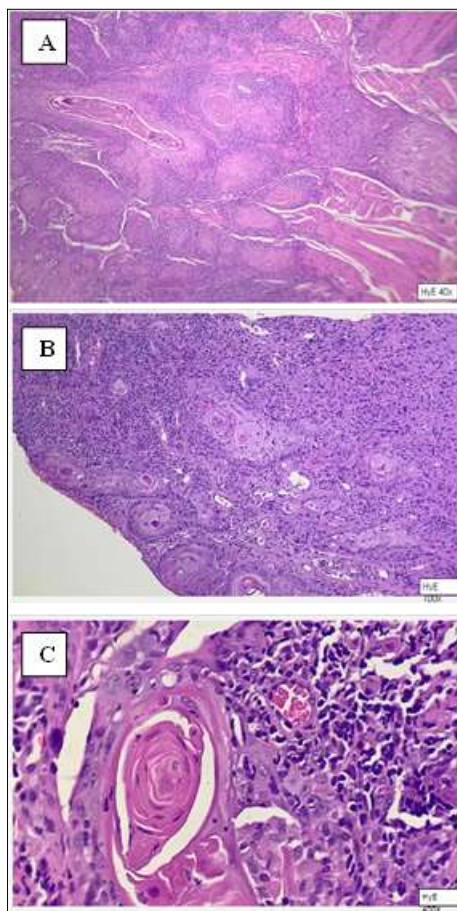
**Fig 9:** Lateral view of the lesión on the right border of the tongue



**Fig 13:** Toluidine blue staining of the lesion



**Fig 14:** Fragments obtained from the biopsy



**Fig 15:** Microscope sections

### Microscopic Description

Microscopic sections reveal segments of mucosa in which a

keratinized stratified squamous epithelium is observed on its surface, acanthotic and hyperplastic with important changes consisting of cellular pleomorphism, nuclear hyperchromatism, enlarged nuclei, few abnormal mitoses, individual keratinizations and horny pearls, some with great formation of keratin, which invades the scarce underlying connective tissue with abundant lymphoplasmacytic chronic inflammatory infiltrate and moderate vascularity. In addition, muscle infiltration is observed (Fig 15).

### Diagnosis

Well-differentiated squamous cell carcinoma.

### Discusión

OSCC represents 90% of oral cavity tumors, presenting around 300,000 new cases and with an incidence rate of 4 cases per 100,000 inhabitants per year [3]. Therefore, the early diagnosis of this condition, or the detection of premalignant lesions that may culminate in it, is crucial.

In the cases presented in this article, the first case coincides with one of the main risk factors, which is the consumption of alcohol and tobacco, as mentioned by Chaturvedi *et al* in their work [9].

Contrary to the second case, which is not in itself a heavy smoker, but we found other risk factors such as periodontal disease<sup>6</sup>, poor hygiene and trauma from the prosthesis that may be causing mechanical irritation that could have contributed to the development of the lesion, as Singhvi concludes in his article [10].

As Bughsan *et al.* comment, OSCC has the potential to metastasize and distant metastases worsen the prognosis and reduce the chances of success [7]. Therefore, a thorough examination, detection of premalignant lesions, observation of their behavior and performance of biopsies, is vital in the diagnosis of these conditions.

We consider that toluidine blue is a diagnostic tool that is not considered definitive but can support the process of taking the biopsy to indicate the best area to take and obtain a better histopathological diagnosis.

### Conclusion

The timely detection of oral cancer and premalignant lesions is a vital issue for the patient's prognosis. Due to the high incidence of OSCC, the dental community is invited to detect, manage, refer and/or diagnose this pathology, for the benefit of the patient.

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