

# Gingivobuccal Squamous Cell Carcinoma: The Keys for an Early Diagnosis

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## ABSTRACT

**Background:** Gingival Squamous Cell Carcinoma have a particularly poor prognostic due to fail of early diagnostic and adequate management. This work aims the report of two cases of Gingival Squamous Cell Carcinoma lately detected and the discussion of different innovations improving the chances of an early diagnostic.

**Method:** We present a 65 years and 82 years old two female patients, both referred to our oral surgery and oral medicine department for concerning lesions in their mandibular gingiva. Extra oral examination revealed in the two cases hypoesthesia in the labial and mental region and homolateral adenopathy. Intraorally, for the first case we detected a crestal ulcero-proliferative lesion of 4 cm resting on an indurated base. For the second case, an exophytic mass is present on the right mandibular side extending from the tooth 42 to the first mandibular molar. Histopathology confirmed the suspected diagnosis of squamous cell carcinoma and a radical surgical treatment joined to reconstruction was performed.

**Results:** Studies on the development of nomograms, artificial intelligence, the detection of accessible biomarkers, are of undeniable value for the improving the chances of detection of a Gingival Squamous Cell Carcinoma leading to optimal management strategies and better outcomes.

**Key Words:** Case report, Gingival carcinoma, Diagnosis, Innovations

## Introduction

Gingival Squamous Cell Carcinoma (GSCC) stands as a rare affliction, primarily impacting the elderly population. Data about this carcinoma are very scarce, especially from Tunisia.

GSCC is an insidious disease, not always having the appearance of a malignancy, presenting a spectrum from exophytic to verrucous to ulcerated lesions. It may mimic periodontal disease or traumatic lesions, risking the delay of the correct diagnosis and institution of appropriate care [1].

The aim of this work was to report two cases of GSCC characterized by late detection, in order to highlight the disadvantages of delayed diagnosis and to discuss the different innovations helping early detection of lesions to improve prognosis and quality of patient care.

## Case Presentation

### ■ Case 1

AA 65-year-old female patient was referred to the oral surgery and oral medicine department for an ulcerated lesion on the attached gingiva of the vestibular side of the edentulous crest. Anamnesis revealed that the patient is a Neffa chewer, a tobacco product, for the last 45 years.

Extra oral examination showed a homolateral hypoesthesia in the labial and mental region and a firm submandibular centimetric painless adenopathy. Intraoral examination revealed a poor oral hygiene, with widespread plaque on the few remaining teeth (Figure 1). The lesion appeared as a crestal ulcerative vegetative exophytic mass, with heterogeneous aspect measuring 4 cm in diameter, bleeding on contact and resting on an indurated base.

**Received:** 01-July-2024, Manuscript No. IJOCS-24-132592; **Editor assigned:** 04-July-2024, PreQC No. IJOCS-24-132592(PQ); **Reviewed:** 19-July-2024, QC No. IJOCS-24-132592(Q); **Revised:** 25-July-2024, Manuscript No. IJOCS-24-132592(R); **Published:** 31-July-2024, DOI: 10.37532/1753-0431.2024.18(4).246

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**Figure 1:** Intraoral view at first visit

An Orthopantomograph and a Cone Beam Computed Tomography showed a poorly defined radiolucent area in the anterior part of the mandibular body indicating a mixed

appearance of the bone (Figure 2 and 3). A malignant lesion was suspected, particularly a GSCC. Consequently, patient was referred to maxillofacial surgery department to better investigation and eventual treatment.

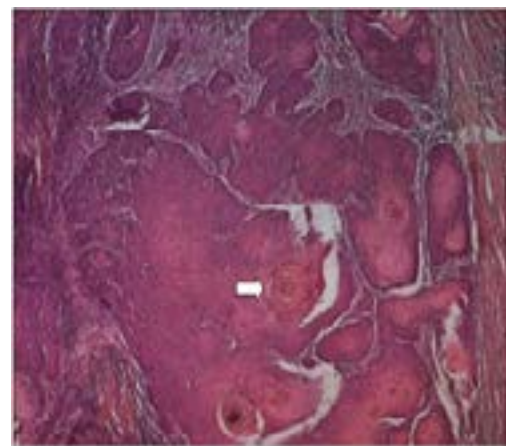


**Figure 2:** Orthopantomograph showing horizontal bone resorption and remaining



**Figure 3:** 3D CBCT image: showing limits of bone resorption

In this department, an incisional biopsy was performed. Microscopic examination showed proliferation and infiltration of atypical cells with irregular nuclei and tendency towards keratinization in the subepithelial tissue (Figure 4). The diagnosis of keratinized, invasive, well differentiated squamous cell carcinoma was made based on these findings. Extensive clinico-radiological investigations were performed to identify potential metastasis. Chest radiography, as well as computerized tomography of the head and neck regions, was conducted. No metastatic lesions or other primary neoplasms were detected. The treatment plan involved the resection of the tumor with a non-interrupting mandibulectomy, involving a few millimeters of the homolateral mandibular floor. The tumor was classified as T4 N0 M0, indicating a large tumor size without nodal involvement or distant metastasis.



**Figure 4:** Biopsy showing proliferation of atypical cells with irregular nuclei and tendency towards keratinization (hematoxylin-eosin staining)

Post-surgery, a reconstruction with a nasolabial flap with an inferior pedicle was performed to restore the defect created by the tumor resection. Functional recovery was facilitated by the installation of prostheses (Figure 5a and 5b).



**Figure 5a:** Intraoral view at 6 months postoperatively



**Figure 5b:** Intraoral view at 6 months postoperatively

## ■ Case 2

An 82-year-old female patient was referred to the oral surgery and oral medicine department for an oral concerning lesion evolving for two months. Extraoral examination showed a right hypoesthesia in the labial and mental region with the presence of homolateral cervico-facial centimetric painless adenopathy. Intraoral examination revealed a poor oral hygiene with the presence of an exophytic mass on the right mandibular side extending from the tooth 42 to the first mandibular molar (Figure 6). The lesion was covered by an ulcerated mucosa with heterogeneous texture and splayed edges, bleeding on contact. The base was indurated. Mobility and teeth displacement in that area were detected.



**Figure 6:** Intraoral view at first visit

The examination revealed also brown macules at the left vestibule floor: On questioning the patient, these marks were those of the Neffa. The retroalveolar cliché showed bone lysis up to the apical third with a mitted appearance of the bone (Figure 7).



**Figure 7:** Retroalveolar cliché showing bone lysis

Through all these signs, a malignant lesion was suspected, particularly a GSCC, in its ulcerative-vegetative form linked to consumption of chewing tobacco (Neffa) since the age of 20. Consequently, patient was referred to maxillofacial surgery department to better investigation and eventual treatment. She underwent biopsy-exeresis of the lesion with filling of the tissue loss with a pectoral flap and radio-chemotherapy. Diagnosis of squamous cell carcinoma was confirmed by anatomopathological examination. Following surgery, the patient was referred for oral cavity rehabilitation and a fluoride gutter confection

before starting radiotherapy (Figure 8).



**Figure 8:** Intraoral and Extraoral views at 6 months postoperatively

### Discussion

Oral Squamous Cell Carcinoma (OSCC) is a significant health concern due to its prevalence and the serious impact it has on patients. It accounts for more than 90% of all malignant lesions found within the oral cavity. The gingival area representing about 10% of all OSCC cases with a preference for the mandible over the maxilla [2].

The etiology of GSCC, similar to other oral cancers, is multifactorial. Tobacco use, alcohol consumption, Human Papillomavirus (HPV) infection, and poor oral hygiene are well-established risk factors. The diagnosis of GSCC requires a high degree of clinical suspicion, symptoms may include a persistent ulcer or growth on the gum, bleeding, localized pain, and in advanced cases, tooth mobility. Biopsy of the suspicious lesion is essential for diagnosis, followed by imaging studies to assess the extent of the disease and to plan treatment. The treatment of GSCC involves a multidisciplinary approach, including surgery to remove the tumor, radiation therapy, and chemotherapy, depending on the stage and aggressiveness of the cancer. The prognosis of GSCC, like other OSCCs, depends on the stage at diagnosis [2].

A delayed diagnosis stands as the most compromising factor in the prognosis of the GSCC and the complexity of its treatment. In these present cases, the GSCC was already well spread when therapy was initiated which required an extensive surgery. Despite notable progress obtained in the diagnosis technics and therapeutic opportunities, the GSCC

still presents a challenging prognosis, with an estimated 5-year overall survival rate of 56% in Europe [1]. The introduction of new innovations to enhance diagnosis has drawn the attention of multiple researchers, in order to help decision-making and improve outcomes, such as:

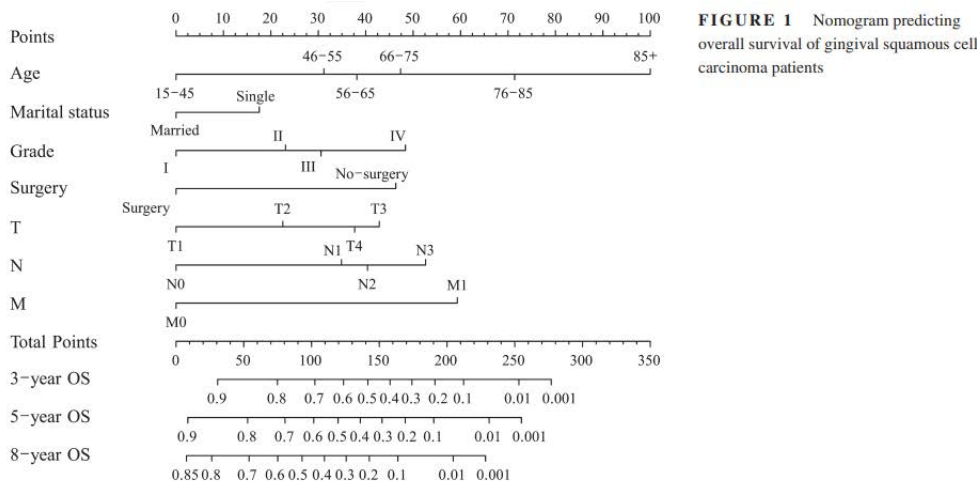
#### ■ The use of nomogram

Nomograms have emerged as a well-defined mathematical prediction tool, commonly utilized in oncology estimate prognosis. It amalgamates multiple crucial factors, helping physicians make significant treatment decisions of various types of cancer including prostate, gastric, esophageal, colorectal and salivary gland cancer. By employing multiple biological and clinical variables, nomograms graphically establish a statistical prognostic model, generating probabilities for clinical events such as cancer recurrence or death for a given individual [3,4]. Recently, authors such as Lei Yan have tried to construct nomograms specific to GSCC with different variables, including marital status, site, grade, surgery, T stage, N stage and M stage (Figure 9) [5].

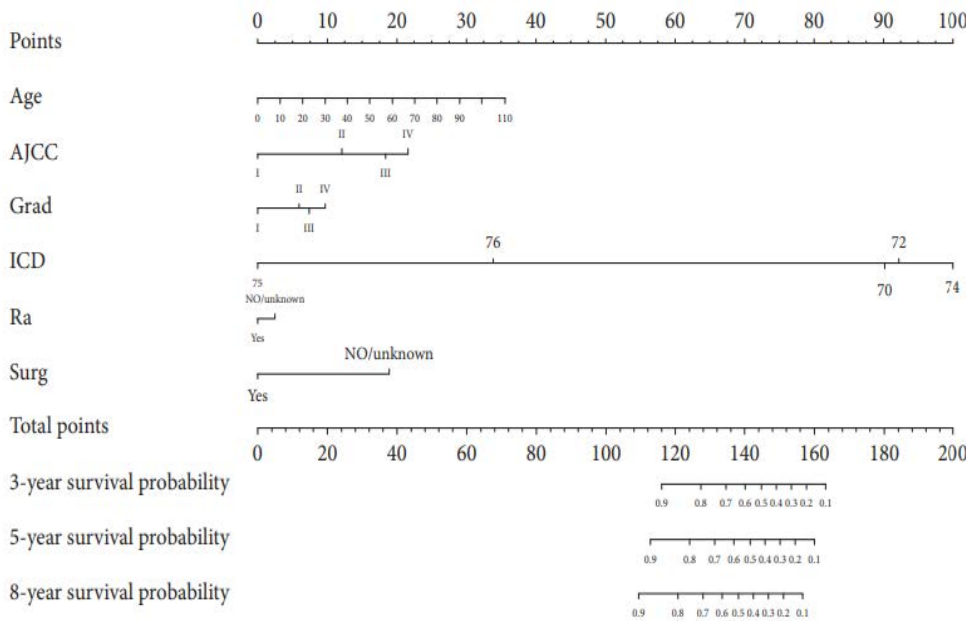
Other Authors like Zheng *et al.* have established a different Nomogram with variables including, age, AJCC stage, tumor grade, histological subtype, radiotherapy status, and surgery status (Figure 10) [3].

Nomograms allows to establish a personalized estimation of the survival rate and makes the decision making clearer with a high accuracy and sensitivity, but these studies remain restrictive specially because they were specific to one race and because they don't include relevant factors important in the development of GSCC such as smoking, alcohol consumption, HPV, and inappropriate oral prosthesis [3,5].





**Figure 9:** Lei Yan’s Nomogram of gingival squamous cell carcinoma



**FIGURE 2:** Nomogram of gingival squamous cell carcinoma.

**Figure 10:** Zheng and al nomogram of gingival squamous cell carcinoma

■ **Artificial intelligence**

The use of Artificial Intelligence (AI) technologies has demonstrated effectiveness in diagnosing various cancers. Recent studies have highlighted the advantageous application of AI in the early detection of oral cancer, particularly with a focus on GSCC. Its versatile applications encompass the analysis of diverse imaging techniques, such as fluorescent, hyperspectral, cytological,

histological, radiological, endoscopic, clinical, and infrared thermal methods leading to superior outcomes and reducing diagnostic errors [6,7].

Current investigations aim to develop AI models specifically tailored for predicting the occurrence and recurrence of Oral Cancer (OC). These models concentrate on forecasting the malignant transformation of Oral Potentially Malignant Disorders (OPMDs), detecting cancer

biomarkers, and researching lymph nodes.

However, these models face limitations due to the little amount of data available, unpredictable image quality, the risk of missing data, and the absence of necessary infrastructure for data storage, building and training AI models [6,8].

#### ■ Biomarkers detection

Uncovering novel biomarkers for cancer screening holds promise in achieving highly sensitive, cost-effective, and non-invasive diagnostic solutions [9].

#### ■ Matrix metalloproteinase

Multiple MMP family members have been investigated as possible biomarkers involved in the spread and metastasis of OC, making them tremendous potential as diagnostic biomarkers. Especially when they are present in more easily accessed biofluids. MMP-11, that is secreted in its active form, has a role in facilitating tumor invasion by degrading collagen, fibronectin, and laminin which makes its expression critical in cancer development and progression [9].

Research on the oral cancer cells and tissue of OSCC patients indicates a frequent association of MMP-2 and MMP-9 with the promotion of infiltrative growth and bone resorption. They are released by cells and necessitate Subsequent activation by proteinases.

MMP-27 serves as a tumor suppressor; decreased MMP-27 expression is associated

with poor differentiation and heightened tumor invasiveness, especially in bone invasion within OSCC [10]. These recent studies open the door to the development of innovative personalized therapeutic strategies for OC, like the use of MMP inhibitors, nanoparticle-mediated targeting of MMP or gene silencing by microRNA, can be designed [11].

#### ■ Neurokinin 3 receptor

In recent findings, the identification of Neurokinin 3 Receptor (NK-3R), which is a member of the tachykinin family expressed in the central nervous system, was identified through pathway analysis as a molecule expressed in osteoclasts induced by the hedgehog signal. Although the expression of NK-3R has been detected in osteoclast and OSCC cells at the bone invasion front, the relationship between NK-3R expression and the prognosis of gingival OSCC patients remains unclear [12].

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#### Conclusion

Given these assumptions, it is crucial for dental professionals to assume a pivotal role in detecting minor changes even in the color of the gingiva and to be up-to-date regarding the innovations reported to avoid delayed diagnosis of such lesions. They should also encourage patients, especially women without conventional risk factors, to seek further examination if a regression of the aforementioned lesions cannot be attested.

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