

Early diagnosis of oral squamous cell carcinoma may ensure better prognosis: a case series

Chiara Bramati¹, Silvio Abati¹, Stefano Bondi¹, Alessandra Lissoni¹, Gianluigi Arrigoni¹, Federica Filipello¹, and Matteo Trimarchi¹

¹IRCCS Ospedale San Raffaele

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Abstract

Oral squamous cell carcinoma (OSCC) is a malignancy with high mortality and morbidity. Early diagnosis and treatment of OSCC and other potentially malignant lesions of the oral mucosa is the clinician's best weapon to improve prognosis, since it greatly worsens as the disease becomes more advanced.

Introduction

In Western countries, oral cancer represents a rather uncommon malignancy, with oral squamous cell carcinoma (OSCC) being most frequent¹. OSCC has high mortality and morbidity², which significantly increases with diagnostic delay³. The most common risk factors for OSCC are well known and include alcohol, use of tobacco (including smokeless tobacco), betel quid chewing, and chronic inflammation^{4,5}, which are for the most part behaviors that can be eliminated. Primary prevention, therefore, consists in educating the population against these behaviors⁶. Once the cancer is present, early diagnosis is the single most important element in improving prognosis, since clinical and pathological staging are the most important factors that influence survival rates⁷. Furthermore, treatment of an early disease, which consists in surgical excision with tumor-free margins, prevents the morbidity that far more invasive surgery for a more advanced disease would imply⁸. The prompt recognition and correct treatment of conditions that present a risk of transforming into cancer, such as leucoplakias⁹ and erythroplakias, also play a very important role in improving the chances of survival¹⁰.

OSCC mostly affects elderly men, although the latest literature seems to suggest a growing incidence in younger patients, especially in tongue cancer, and in particular when linked to chronic mucosal trauma caused, for instance, by sharp dental elements¹¹. Furthermore, some authors suggest that younger patients bear a more aggressive disease, with higher locoregional recurrence rates and worse prognosis¹².

The following case series reports four cases in which early diagnosis was essential in ensuring good prognosis to all individuals, as all are in good health and disease-free at the time of writing.

The present article was approved by the Ethics Committee of San Raffaele Hospital (20210422), in accordance with the Declaration of Helsinki. All patients gave their informed consent.

Case presentation

Case 1

F.F., a 32-year-old woman who was referred to our dental clinic for a burning sensation in correspondence of the left aspect of the tongue. Her past history included diagnosis of skin melanoma (Breslow stage I) about a year prior, for which she had undergone surgical excision.

Clinical examination revealed the presence of a solid, tender, ulcerated lesion of the left tongue border, with dyskeratotic areas (Fig. 1). A biopsy of the lesion was carried out, with histologic examination showing the presence of a G2 squamous cell carcinoma, even though the patient apparently showed no risk factors, as she was neither a smoker nor a heavy drinker. Contrast-enhanced MRI confirmed the presence of a highly vascularized solid lesion, confined to the lingual body, without infiltration of the adjacent muscles and mandible.

The patient consequently underwent a partial marginal glossectomy with CO₂ laser (type II glossectomy sec. Ansarin)¹³ and sentinel lymph node biopsy. Histologic examination confirmed the presence of a G2 SCC (Fig. 2), pT2 pN0 lesion.

At one year postoperative, the patient is currently disease free (Fig. 3), as revealed by periodic clinical examination and contrast-enhanced MRI.

Case 2

G.B., a 61-year-old man with a history of active drinking (half a litre of wine per day). During a routine dental examination, an erythroleukoplakic lesion of the left retromolar area was identified (Fig. 4). Given the risk factors presented by the patient and the appearance of the lesion, it was decided to perform an immediate biopsy. Histologic examination showed the presence of severe dysplasia.

Even though histologic examination did not show the presence of cancer, given the high risk that lesions such as erythroleukoplakia carry, it was nevertheless decided that the patient undergo surgery.

The lesion was excised by CO₂ laser. Histology showed the presence of a micro-focal T1 G2 squamous cell carcinoma in the context of a severely dysplastic mucosa (Fig. 5).

Almost two years after surgery, the patient is undergoing regular follow-up and is disease-free.

Case 3

T. D., a 43-year-old man presented with a leukoplakic lesion of the right tongue border (Fig. 6). A biopsy was carried out, showing a verrucous proliferation with atypia, which was dubious for neoplasia.

Contrast-enhanced MRI confirmed the presence of the lesion, which did not appear to infiltrate the intrinsic muscles of the tongue or neighboring structures.

It was thus decided to surgically excise the lesion by transoral mucosectomy with a CO₂ laser (type I glossectomy sec. Ansarin)¹³. Histology showed the presence of a G1 squamous cell carcinoma (1 cm in greatest dimension) in the context of a verrucous hyperplasia with lichenoid chronic inflammation (Fig. 7).

Two years after surgery, the patient is disease free, as shown by periodic clinical examinations and contrast-enhanced MRI.

Case 4

L. D., a 24-year-old woman presented with a leukoplakic lesion of the right border of the tongue (Fig. 8), progressively growing in size. The lesion was biopsied on multiple occasions. The latest histological examination showed the presence of severe dysplasia, while the previous one showed only moderate dysplasia. Given that the lesion was constantly increasing in size (reaching an extension of 2 cm circa) and that the grade of dysplasia seemed to be progressively worsening, it was decided to surgically intervene.

The lesion was excised transorally by CO₂ laser. Histologic examination showed the presence of inflammation and keratosis (Fig. 9). Two years after the excision, the lesion has not recurred (Fig. 10).

Discussion

Oral cancer is an extremely malignant condition, with a very high risk of mortality and morbidity, albeit not common in Western countries. Diagnostic delay can contribute greatly to poor prognosis of the disease, since up to 50% of oral malignancies are diagnosed in a very advanced stage (III – IV), which translates

into poor prognosis; this underlines the importance of early diagnosis and prevention of disease progression³. Overall, 5-year survival is estimated at around 50%¹, while for advanced stage OSCC it decreases to 30%¹⁴. Clinical and pathological stage at presentation represents the single most important prognostic factor, with the presence of lymph node metastases being the most powerful predictor of outcome¹⁵ since the presence of a single node metastasis confers up to a 50% decrease in overall survival¹⁶.

Up to 33% of patients present with occult cervical disease, undetectable by imaging techniques (mainly CT and MRI)¹⁷; the use of sentinel node biopsy (SNB) represents an excellent solution in cases of T1-T2 tumors with a clinically N0 neck^{17,18}. SNB is an extremely valuable method in detecting occult node metastases in head and neck cancer, with a negative predictive value of about 95%, and represents a solution for the management of a clinically N0 neck¹⁷, as it can better select patients for which nodal dissection is required and avoid unnecessary surgery¹⁸. SNB represents an alternative to management of the neck according to DOI, as lesions with DOI > 4 mm can be either treated with an upfront neck dissection or kept under close follow-up for neck metastases¹⁷.

Risk factors for oral cancer include heavy use of tobacco, alcohol drinking, and betel quid chewing⁶. Chronic mucosal trauma, originating from poor oral hygiene, poor dentition, missing teeth or ill-fitting prosthetics¹⁹, has been postulated to be an etiological factor for oral cancer; this may be particularly true for younger patients presenting with no other risk factor for OSCC (mainly use of tobacco and alcohol)¹⁴, as up to 30% of nonsmokers and nondrinkers presenting with OSCC present with some kind of dental abnormality in proximity to the tumor²⁰. HPV may have a role as a risk factor, although it cannot be considered an independent prognostic factor²¹, as for oropharyngeal cancer²².

Since oral cancer can be considered a highly preventable disease, ideally screening campaigns should educate the population to eliminate risk factors for oral cancer, mainly tobacco smoking and alcohol consumption. This, however, has not proven to be effective. Additionally, even though cancer awareness has greatly increased in the last decades, the percentage of patients seeking medical attention with an advanced stage disease has not changed significantly in the last 40 years²³. Once the carcinogenic process has been established, the best weapon a clinician has against the disease is early diagnosis. Unfortunately, unlike other more frequent cancers (i.e. colorectal cancer) a population-based screening program for oral cancer does not exist and would not be feasible or cost-effective²⁴. A group of oral conditions and diseases are known to be precursors to oral cancer; these include leucoplakias, erythroplakias, oral lichen planus, and chronic inflammatory lesions²⁵. The prompt identification of these lesions and their treatment is of the utmost importance, as it represents a means of pre-venting cancerous transformation²⁶. As not every premalignant lesion of the oral cavity transforms into cancer, the decision to excise the lesion or keep the patient under close follow-up must be made according to clinical and histopathological findings^{27,28}.

As proposed by the World Health Organization, any lesion of the oral mucosa that does not regress within two weeks after elimination of the possible cause (i.e. sharp teeth causing trauma) must be biopsied²⁹. The identification of any suspect lesion of the oral mucosa starts with clinical examination, which consists in visual and tactile inspection of the oral cavity and can be carried out, for instance, in the context of a dental appointment^{7,30}. Biopsy remains the gold standard in diagnosis, while a series of other tools are starting to be used as aids in diagnosis; these include toluidine blue staining, autofluorescence imaging, and salivary biomarkers for point-of-care testing^{6,31}.

In all four cases presented herein, diagnosis was established starting from a simple clinical inspection carried out in the context of a dental appointment, which was nevertheless able to guarantee good prognosis. All lesions were thus diagnosed and excised in the early stages, making it possible to considerably reduce the morbidity associated with the disease and its treatment when in an advanced stage. In case 1, after the diagnosis of OSCC was made, it was also decided to carry out a sentinel lymph node biopsy. As histological examination showed the absence of any node metastases, it was possible to avoid further unnecessary surgery on the neck, while still obtaining oncological radicality. In case 3, however, the neck was managed according to DOI: pre-operative MRI showed the presence of a lesion with a maximum DOI of 3 mm, so that the surgical excision was carried out without performing a neck dissection. Onco-logical radicality was achieved

nonetheless, as periodical clinical examinations and MRI imaging still demonstrate no recurrence and a NO neck at two years postoperative.

In case 2, the decision to excise the erythroplakic lesion was taken before the diagnosis of OSCC was made, as the initial histology only showed the presence of high-grade dysplasia. As is well known, erythroplakia is the single most dangerous pre-cancerous lesion of the oral cavity, as up to 85% if erythroplakias show histological signs of carcinoma once biopsied or excised^{32,33}. Indeed, in our case, histological examination of the entire lesion revealed the presence of a G2 squamous cell carcinoma, which was thus eradicated in its very early stages, avoiding the need for far more extensive surgery had the lesion been allowed to grow in size. Case 4 represents an example of a lesion (leucoplakia) that is not cancerous in itself, but which carries a risk of transforming into cancer³¹, even though not as high as that of erythroplakia³². Given that the lesion was rapidly increasing in size and its grade of dysplasia rapidly worsening, it was decided to completely excise the lesion surgically. Histological examination did not show the presence of cancerous foci; nevertheless, by excising the lesion in its entirety, the need for periodic biopsies was eliminated, while eradicating the risk of malignant transformation.

Conclusions

OSCC is an extremely malignant condition, with very poor prognosis when diagnosed at an advanced stage. The best weapon to improve prognosis is to diagnose oral cancer as early as possible. Diagnosis starts with a simple visual and tactile examination of the oral cavity, which can be carried out in the context of a dental appointment. The cases presented herein show how early diagnosis, starting from a simple examination of the oral cavity, can ensure very good prognosis.

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Figure legends

- **Figure 1.** Case 1: pre-operative appearance of the lesion
- **Figure 2.** Case 1: squamous cell carcinoma associated with keratin pearl formation, infiltrating the intrinsic lingual muscle. (H&E)
- **Figure 3.** Case 1: fully healed post-operative appearance of the tongue
- **Figure 4.** Case 2: erythroleukoplakic lesion of the left retromolar area
- **Figure 5.** Case 2: squamous cell carcinoma with basaloid features, demarcated by a mild layer of lymphocytes and plasma cells (H&E).
- **Figure 6.** Case 3: a vast leukoplakic lesion of the right tongue border (2.5 x 2.5 cm) with a squamous cell carcinoma of 1 cm in greatest dimension in its context.
- **Figure 7.** Case 3: well differentiated squamous cell carcinoma characterized by finger-like growth, infiltrating the superficial layers of the intrinsic lingual muscle. (H&E)
- **Figure 8.** Case 4: pre-operative appearance of the leukoplakic lesion
- **Figure 9.** Case 4: Superficial resection of squamous epithelia showing keratosis and dyskeratosis with mild nuclear irregularity of the squamous epithelia. (H&E)
- **Figure 10.** Case 4: post-operative, fully healed, appearance of the tongue











