

Impact of Delay on Diagnosis and Treatment of Oral Squamous Cell Carcinoma: Three Cases Report

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Abstract

Oral squamous cell carcinoma (OSCC) can be present with a wide range of clinical appearances, particularly during its early stage that may not be considered suspicious by clinicians, which can cause a delay in its diagnosis and treatment. In this paper, the cases of three patients are reported: 41-year-old female, a 45-year-old male and a 53-year-old male with persistent and painful oral ulcers on the tongue and difficulties in swallowing for approximate 9 to 12 month that did not respond appropriately to the previous treatment, without a clear diagnosis. Clinically, premalignant and malignant lesions may sometimes resemble each other. In first case, dysplastic changes should be considered as the signs of premalignant lesions that need to be observed periodically. The malignant lesions were found in the other two cases. A delayed diagnosis of OSCC could lead to a progression to more advanced stages, more extensive treatments, poorer survival and greater psychological morbidity. Therefore, it is scientifically and socially relevant to increase the knowledge and awareness concerning the early symptoms of OSCC among general public and dental health professionals that can have a great impact of the disease.

The finding derived from these three cases highlight the caution that needs to be exercised in clinical assessment of OSCC from another chronic ulcer with similar features.

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Introduction

The most frequent malignancy of oral cavity is oral squamous cell carcinoma (OSCC).^{1,2} As OSCC was found in a wide range of clinical appearances, it tends to be overlooked by dental professionals. Consequently, the situation prescribed would lead to a delay in its diagnosis and treatment. The clinical stages (TNM), particularly a timely diagnosis, play an essential role for the survival and prognosis of patients.¹

The most common site of OSCC is on lateral borders of the tongue, the floor of mouth, buccal mucosa, gingiva and soft palate.³ The clinical presentation of oral mucous may present in a variety of forms which include red/white or mixed lesions, white plaques, erythema, ulcer

with indurated raised margin, and verrucous growth.⁴ However, these lesions typically produce no prominent signs and discomfort until they progress. Some lesions may progress to a mucosal growth (mass) and ulceration; the patients may have lymph node involvement, discomfort, malodor, difficulty speaking, chewing and swallowing, and bleeding at the site of the lesion.³ Additionally, OSCC lesions may arise without detectable pioneer lesions, and if they do, these preliminary lesions may look clinically innocuous and can be assumed benign in many cases.⁴

Early diagnosis and treatment of OSCC is important to avoid complications such as metastasis to other regions.⁵ The probability that delayed diagnosis patients present an advanced stage tumor at diagnosis is approximately 30% higher than non-delayed diagnosis patients. Hence, educational interventions aiming at an early recognition of oral cancer signs and symptoms may be considered for high-risk populations.⁴

Healthcare workers (physicians and dentists) also play a role in diagnostic delay on

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oral cancer.⁴ They need to increase their capacity to recognize oral malignant and premalignant lesions in order to obtain an early definitive diagnosis of oral cancer.⁶

Case Report

The first case, a 41-year-old female was admitted to Oral Medicine Department with complaint of painful ulcers on the right lateral of the tongue for nine month. The ulcers had been treated with policresulen for a month. She also came to general dental practitioner (GDPs) for treatment and was given mouthwash. However, the ulcers became larger, indurated with irregular raised borders, and more painful than before.

Extraoral examination revealed lymphadenopathy on her right submandibular gland, pain and no abnormalities on her lips. Intraoral examination showed that there were painful ulcers, white plaque on the right lateral of the tongue rounded by erythema (Figure 1A). Gangren radix on 14 was also found in this patient. Based on the anamnesis and clinical findings, oncology was referred in order to conduct the biopsy and treat the ulcer with chlorhexidine gargle 0,1%.

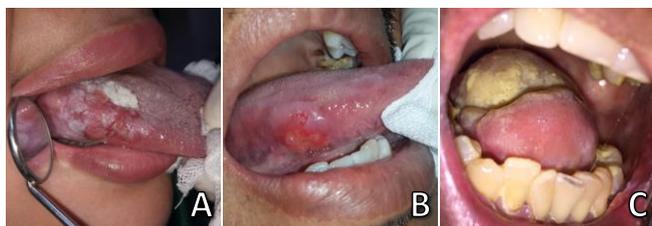


Figure 1. Clinical feature and extra oral examination of (A) case 1, (B) case 2, (C) case 3.

The histopathological assessment of the lesions told that papillomatous squamous epithelium, acanthosis, dysplasia half of nuclei, stratification and maturation are relatively normal (Figure 2A). The diagnosis of this first case was papilloma with dysplasia and the treatment required was a surgery.

The second case, a 53-year-old male was admitted to Oral Medicine Department with complaint of persistent and painful ulcers on the right lateral of the tongue and difficulty in swallowing for around nine month. Patient had treated the ulcers with policresulen but no signs of improvement found on the patient.

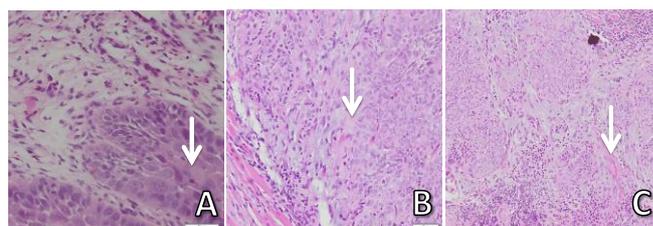


Figure 2. Histopathological feature of (A) Case 1, showed an increased nucleus-cytoplasm ratio; (B) Case 2, showed polymorphic nuclei and hyperchromatic mitosis; (C) Case 3, showed polymorphic nuclei and hyperchromatic mitosis.

Extraoral examination revealed lymphadenopathy on his right submandibular gland, and no abnormalities on his lips. Intraoral examination showed that there was erosive lesion of the right lateral margin of the tongue with surrounding areas of hyperkeratinisation, and the borders were indurated on palpation (Figure 1B). Gangren radix with sharp edge on 26 and 36 was also detected on this patient. Based on the anamnesis and clinical findings, oncology was referred in order to conduct the biopsy and treat the ulcer with chlorhexidine gargle 0,1%.

Biopsy result of the second case showed hyperplastic squamous epithelium, acanthosis, tumor mass with polygonal cells, polymorphic nuclei and hyperchromatic mitosis (Figure 2B). The diagnosis was OSCC T2N1M0 stage III and the treatment was surgery followed by radiation therapy and chemotherapy.

The third case, a 45-years old man was referred from Internal Medicine to Oral Medicine Department with complaint of pain ulcer on the right lateral of the tongue for one year. His medical history revealed that he had no systemic disorder. He had habits such as smoking and alcohol intake. Intraoral examination revealed an ulcerated, hyperemic enlargement with an irregular surface (Figure 1C).

An incisional biopsy was taken and histopathological examination demonstrated hyperplastic squamous epithelium, acanthosis, tumor mass with polygonal cells, polymorphic nuclei and hyperchromatic mitosis (Figure 2C). The diagnosis was OSCC stage IV with hepar mestatase. The patient has been treated surgery followed by radiation therapy and chemotherapy.

Discussion

Three steps of diagnostic delay of OSCC shown by Figure 3 are categorized as patient, professional and system delay. OSCC patients usually wait for 3 – 5.4 months before consulting with dental professional after self-discovery of signs and symptoms of oral cancer, which is called patient delay. This delay is related to the difficulty experienced by patients in perceiving such signs and symptoms as harmful, whereas they are usually dismissed as a minor oral disease, e.g., trauma, infective process, disorders related to dentures or other generic, non-dangerous dental conditions.⁷ Clinically, early forms' characteristic presentation of oral cancers in most cases is the form of persistent ulcers with indurated margins.⁸

The second step of diagnostic delay is professional delay (14 – 21 weeks). This delay is defined as the time from patients' "first examination of dental professional" to final diagnosis, including referral to specialist, time to biopsy or time to treatment.⁴ Most of the patients thought that "dentists are for teeth and gum" so that only few OSCC patient consulting with dental professional. Dentist may also delay the diagnosis because providing limited oral examination and not identifying suspicious lesions.⁴

System delay is the last step of diagnostic delay. This delay occurs not solely because of patients' actions but system factor such as accessibility, availability and cost of the treatment. Barriers in the health care system, resource availability and issues of healthcare economics may result in a scheduling delay.⁴ Only 40% of OSCC patients with advanced oral cancer have access to primary health care services.⁴

The patient of the first case indicated painful ulcers on the right lateral of the tongue for approximately nine months. She also tried to treat herself with policresulen for a month. The patient had patient delay (3 months) since she considered ulcers as harmless signs/symptom. Professional delay (6 months) took place when the general dental practitioner (GDPs) was also not able to identify the suspicious lesion and only provided mouthwash to the patient.

Ulcers considered as harmful signs after the ulcers not resolved for nine months. Doctor established diagnosis by biopsy and showed papillomatous squamous epithelium, acanthosis, dysplasia half of nuclei, stratification and maturation are relatively normal. The diagnosis was papilloma with dysplasia and the treatment recommended was a surgery. Papilloma is caused by human papillomavirus (HPV), which is one of the important etiological factors for OSCC and may play role in oral tumor progression.⁹

Patient of case 2 and 3, in the present series with a persistent oral ulcer on the right of lateral tongue. The lateral tongue being the most frequent situation (80%), followed by ventral and dorsum.¹⁰ The lateral border of the tongue and the floor of the mouth combine to form a horse shoe shaped region in the oral mucosa as highly risk for cancer development and also as a bad prognostic area.¹⁰ Both of them had been a smoker for a 15-20 years and alcoholic. The major risk factors for OSCC are smoking and alcohol consumption.¹¹

They treated themselves with policresulen for a month. Policresulen is a topical hemostatic and antiseptic with a highly acidic pH, which results in a marked bactericidal action on the most common pathogens as well as efficacy against *Candida albicans*.¹² The favorable effects of policresulen are attributed to its highly acidic characteristics, which cause the selective coagulation of necrotic or pathologically altered tissues while leaving healthy tissues unaffected. Therefore, policresulen is used to treat infections of the mucous membranes and eruptions on the tongue.¹²

The two of patient was diagnosed with OSCC in advanced stage (stage III and IV) and had been treated with surgery followed by radiation therapy and chemotherapy. The clinical presentation of OSCC in advanced stages is usually clear suspicion of malignancy.³

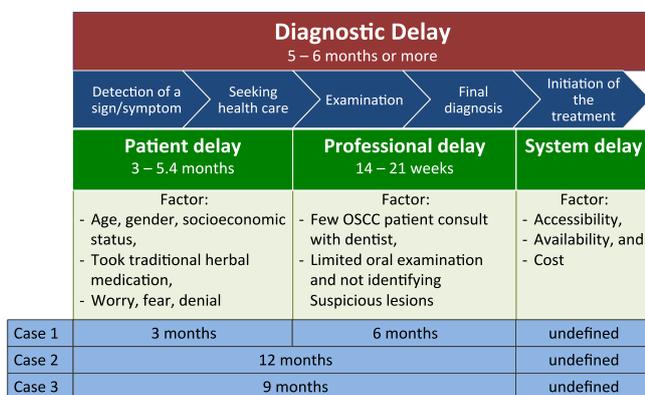


Figure 3. Component of diagnostic delay⁴ and diagnostic delay of case report.

Diagnostic delay could lead OSCC to advanced stages that need more extensive treatment, poorer survival and greater psychological morbidity. Survival duration for patient in early stage can be 5 years, but this survival duration decreased in advanced stage with only 6 months until 1 year.¹³

One of the most useful prognostic indicators of malignancy is the severity of epithelial dysplasia which is assessed with a biopsy.¹⁴ Biopsy allows histological examination and categorization according to features defines by World Health Organization, classically into mild, moderate and severe.¹⁴

Beside biopsy, detection of OSCC can be done by detect expression of p16 and p53. P16 and p53 are tumor suppressor genes that are increased following OSCC stage of malignancy.¹⁵ Because of that characteristic, p16 and p53 can be used as potential markers for early detection in OSCC.¹⁵

Conclusions

Clinically, premalignant and malignant lesions may sometimes resemble each other. Thus, the diagnosis should be confirmed by biopsy. Dysplastic changes should be considered as the signs of premalignant lesions that need to be observed periodically. The delay in diagnosis of OSCC can be due to the patients' ignorance of early signs and symptoms of disease, dental health professionals may overlook the risk of possible malignancy, and misdiagnosed because of its variable and innocuous clinical appearance.

Delayed diagnosis of OSCC could lead to a progression to more advanced stages, more extensive treatment, poorer survival and greater psychological morbidity. There is a need to increase knowledge and awareness of the early signs and symptoms of OSCC among general public and dental health professionals that can have a great impact of the treatment of the disease in the future.

Declaration of Interest

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