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CASE REPORT

Oral Squamous Cell Carcinoma in A Younger Woman with Lack of Known Risk Factors

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Abstract

Background: Oral ulcer is a common oral mucosal lesion and arguably the most challenging one to manage because of its various predisposing factors. The public refers to all types of ulcers in the oral cavity as stomatitis, although it can lead to various diagnoses, including malignancy. **Case Presentation**: This case report aims to discuss obstacles in diagnosis for a case formerly underdiagnosed as stomatitis in a young adult woman with a definitive diagnosis at the end as squamous cell carcinoma of the left tongue. **Case management**: Initial therapy involves eliminating the infection, which is achieved through local therapy using antiseptic mouthwash combined with chlorine dioxide gel to reduce the size of the lesion and alleviate the pain. During the second visit, there was a significant improvement in the ulcer size, but the area of induration persisted. The patient was then educated and informed about the suspicion of malignancy and referred for a biopsy. **Conclusion**: Oral ulcer presented with induration should be managed immediately, including referral for biopsy of the lesion and symptomatic relief. Although the ulcer significantly improved in size after infection control, the induration presented should raise suspicion of malignancy, and a biopsy is mandatory to obtain a definitive diagnosis without delay.

Keywords: OSCC, Young female, Chronic ulcer, Infections

INTRODUCTION

The oral cavity is a vulnerable area due to its multifunctional roles in digestion, respiration, and communication. The mucous membrane lining the structures in the oral cavity extends from the vermillion border of the lips and labial mucosa anteriorly to the palatopharyngeal folds posteriorly and has functions including protecting the underlying tissue from mechanical, chemical and biological stimuli, secreting essential substances and sensory functions related to the perception of temperature, touch, pain and taste referred to oral mucosa.[1]

In the general public, all types of lesions in the oral cavity are commonly referred to as stomatitis, oral ulcers or canker sores. Ulcerations are defined as loss of integrity from the epithelium to the lamina propia. It is estimated that around 40% of the population experiences canker sores, which can cause taste disturbances and difficulty while speaking, eating, and swallowing, resulting in a lack of appetite or even interfering with the ability to perform oral hygiene procedures.[2] Furthermore, it is one of the main reasons people seek treatment.[2]

Ulceration may be inflicted by various factors, including accidental biting, the friction of sharp tooth surfaces due to residual roots or caries, broken fillings, hot temperatures, chemical trauma, sharp restoration edges, nutritional deficiencies (iron, folic acid, and B12), manifestations of certain systemic

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diseases, malignancy, or oral cancer.[3] Therefore, correctly identifying the aetiology and diagnosis of oral ulcers will support the provision of appropriate therapy for patients.

Oral squamous cell carcinoma (OSCC) usually presents as persistent oral ulcers. OSCC is the most common malignant epithelial neoplasm affecting the oral cavity. Worldwide, oral cancer accounts for 2%-4% of all cancer cases.[4] In some regions, such as Pakistan and India, the prevalence of oral cancer is higher, reaching 10% of all other cancers. During the period between 2004 and 2009, more than 300,000 new cases of oral and oropharyngeal cancer were diagnosed worldwide. During the same period, more than 7,000 people affected by these cancers died from them.[4] All the fatality was caused mainly by late diagnosis of this condition. In other words, for the appropriate and timely management of oral cancer, detection, early-stage diagnosis, and immediate referral are essential. Here, we present a case that challenges the immediate referral.

CASE REPORT

A 41-year-old female patient came to the Oral Medicine Department, Gambiran Hospital Regional Kediri, with the main complaint of stomatitis that had been present for two months without any history of tobacco smoking, alcohol drinking or betel nut chewing. On examination, her general health was excellent. The past medical and social histories revealed no significant findings. Extraoral examination revealed enlarged left submandibular and submental lymph nodes with a rubbery consistency but no pain on palpation.

An intraoral examination showed an irregular roll-up edge ulceration with a necrotic centre on the top of an exophytic mass on the lateral tongue adjacent to 35-38. The surrounding mucosa was whitish red, with clear boundaries and raised edges. The dimension is approximately 4 cm, indurated and was painful with palpation (Figure 1). There were no local sources of irritation, such as sharp tooth surfaces, dentures or chipped old fillings, that were detected during inspection. Based on the anamnesis and clinical examination, this patient was highly suspected to have an ulcerative lesion associated with oral squamous cell carcinoma. Moreover, considering the rolled edge and edematous surrounding, the differential diagnoses of Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) and Eosinophilic Ulcer were also noted.

During this first visit, the patient was treated to eliminate the suspected focus of infection by cleaning tartar and receiving antiseptic mouthwash and gel with a chlorine dioxide content. Communication, Information, and Education were also provided to the patient, including information about the possibility of her oral ulceration leading to malignancy, so a biopsy was necessary to establish the diagnosis. A discussion about possible causes of the lesions and widely known carcinogenic agents was also conducted. The patient was also provided with information on a healthy lifestyle, including avoiding exposure to cigarette smoke and limiting consumption of ultra-processed foods, foods prepared using burning techniques, and those containing preservatives. The patient was then scheduled for a follow-up visit one week after the initial visit. At this first visit, the patient declined for biopsy procedures and proceed to use the prescribed medication only.

Figure 1. Oral chronic ulceration of the left lateral tongue with roll edge and induration. The centre of the ulceration showed a necrotic area and a whitish-yellow mass.

A week after the first visit, the patient had a follow-up appointment. Upon examination, the left submandibular and submental lymph nodes were palpable, painless, and enlarged, with a rubbery consistency. The intra-oral examination revealed that the lateral lingual ulceration with pain had decreased compared to the initial visit (Figure 2). The patient was pleased with the result, as the ulceration had significantly improved, according to the patient. The therapy administered during the second visit consisted of applying antiseptic mouthwash and gel containing chlorine dioxide, along with vitamins rich in antioxidants. The patient was re-educated about the possibility of malignancy and referred to undergo a biopsy.

Figure 2. On the second visit, the patient reported a reduction in pain, and further education about the suspect malignancy was provided. The patient finally agreed to the biopsy.

A week following the second visit, the patient returned for follow-up. Excellent progress was seen on the lesions. Painless ulceration accompanied by an exophytic mass on the lateral tongue adjacent to 35-38 looked smaller, reduced by 1 cm in diameter compared with the second visit, with a mixed whitish red colour, irregular shape and raised edges (Figure 3). The patient insisted that her canker sores had improved and requested further medication treatments. At this stage, the patient was informed that although the mouth ulcers had improved significantly, the induration in this case indicated the potential that lead to malignancy. The patient finally agreed to have the biopsy.

Figure 3. The tumour showed a significant reduction in size and symptoms.

At the fourth visit, the patient finally came in with a biopsied site on her tongue. Microscopically, there were pieces of squamous epithelial lined tissue with ulceration and tumour proliferation. The tumour was arranged in a syncytial and hive pattern, consisting of cellular proliferation of oval, round nucleated polygonal anaplastic epithelial cells, mild to moderate pleomorphic features, vesicular chromatin, prominent nucleoli, broad eosinophilic cytoplasm, partly with intercellular-bridging, mitotic

13/10 HPF (High-power Field). No keratin pearl formation was seen in the sections. The tumour grew invasively into the stroma of the fibrous connective tissue with a dense scattering of neutrophil and mononuclear inflammatory cells up to the superficial muscle tissue. There was perineural invasion, no lymphovascular invasion. The tumour distance to the nearest resection margin was undetermined, which meant tumour cells were still left. The conclution of biopsy interpretaion reported poorly differentiated oral squamous cell carcinoma. The patient was explained about the biopsy results and then referred to surgical oncology. Currently, the patient is undergoing tongue hemisection and chemotherapy.

DISCUSSION

The most common malignancy in the oral mucosal epithelium of oral squamous cell carcinoma (OSCC) comprises almost 90% of all oral cancers. Patients usually complain of impaired swallowing, pronunciation, altered taste sensation, and mouth ulcers that do not heal. Patients usually recognise abnormalities through the presence of a persistent sore or mass, symptoms that affect eating and speaking functions, or pain when chewing.[4,5]

Tumours in the oropharyngeal area will show advanced symptoms according to their anatomy, for example, difficulty eating or even pain in the ear area. OSCC can be initiated from oral lesions that have the potential towards malignancy (oral potentially malignant disorders). Some of the known risk factors that cause this condition are alcohol use, smoking habit, human papillomavirus infection and betel nut chewing.[6]

The incidence of OSCC is currently skewed towards younger populations, which may be related to lifestyles such as smoking (or exposure to cigarette smoke) and drinking alcoholic beverages.[7] Based on risk factors, women have less potential than men. Still, in reality, a small percentage of patients, mostly women, demonstrate a higher proportion of oral cavity tumours without smoking and alcohol consumption.[8,9,10,11] Recently, cases of malignancy in the oral cavity that occur in the United States are mostly in young adult women who do not have risk factors. Various theories have been put forward regarding this, including genetic factors, periodontal infections, and lack of vegetable and fruit intake.[12]

Epithelial cells exposed to risk factors for OSCC will genetically mutate and produce neoplastic sites in the mouth or as a trigger for the development of precancerous lesions. The most common areas of the oral cavity where OSCC is usually found are the lateral border of the tongue, followed by the floor of the mouth and then the lower lip.[13]

Cigarettes are one of the factors that play an essential role in the occurrence of OSCC. Benzopyrene, nitrosamines and aromatic amine compounds are three chemicals contained in cigarette smoke that play roles as carcinogenic substances. In this case, the patient stated that she did not have a smoking habit but admitted that her daily activities were close to cigarette smoking. Passive smokers have a three times greater risk of oral cancer than individuals without exposure to cigarette smoke. Other possible risk factors in this case are poor oral hygiene, poor nutrition, genetic predisposition, human papillomavirus (HPV), ultraviolet radiation, Hepatitis C and Epstein-Barr Virus (EBV).[14]

Poor oral hygiene, although not a direct factor in triggering cancer in the oral cavity, can be a reservoir for carcinogenic substances. People with dental plaque will have an increased formation of nitrite and nitric oxide in the mouth. Nitrate reaches the salivary glands through blood circulation and is then secreted into the oral cavity and partially reduced to nitrite by oral microflora. Nitrite and nitric oxide that combine with bacterial enzymes in the oral cavity will form nitrosamines, the same carcinogenic substances present in cigarette smoke.[15]

Nutrition is also an essential component in the occurrence of OSCC. Certain foods can protect the body against oral cancer and stimulate healing effects. Examples of foods that rich in antioxidants are vegetables, Curcuma, green tea and many different kind of fruits. Meanwhile, so-called pro-inflammatory dietary foods such as red meat or fried foods contribute to the growth, development and spread of oral cancer. Pro-inflammatory foods or diets can increase the risk of oral cancer through several mechanisms, including the production of bioactive molecules in the cancer tumour environment, such as CRP (C-Reactive Protein), IL-6, and homocysteine.[16]

In this case, the patient had moderate oral hygiene, and the patient also admitted that she had abandoned her diet because she had been taking care of her husband, who had dialysis and had to travel a long distance for the treatments. Vegetables and fruits were minimally consumed, and the diet was most likely instant food with meat. The improvement in this patient's lesions is likely related to oral

hygiene care and topical antiseptic medications that maintain oral hygiene and minimise oral bacteria. Antioxidant supplementation also helped the lesions progress in a more favourable direction. However, such clinical improvement should be treated cautiously for all the clinical appearances leading to malignant characteristics.

The other aspect that has not been thoroughly explored is stress. The patient has been the carer of her chronically sick husband for a while. It was indeed mentioned that chronic stress may contribute to the progression of cancer.

The process of cancer development will undergo an evolutionary process from the initial lesion and pass through various phases of preneoplastic damage. This carcinogenesis process may be manifested as precancerous lesions such as erythroplakia, leukoplakia, oral submucosa fibrosis and other OPMD lesions. However, not all OPMD or reactive lesions will develop into malignancy in the oral cavity. Epithelial reactive changes and preneoplastic changes are processes that occur before the formation of invasive carcinoma. Hyperkeratosis, hyperplasia and acanthosis are examples of epithelial reactive changes, while mild-moderate-severe dysplasia is an example of preneoplastic changes. The process of squamous cell changes in the form of dysplastic proliferation on the surface that progresses to the subepithelial basement membrane will damage the underlying tissue, called metastasis. Metastasis is directly related to the differential extent of tumour cells, similar to the architecture of neoplastic tissue and normal epithelium.[17]

The cancer stage is a way of describing how extensive the cancer is. The stage is related to its size and spread to the surrounding tissue areas. The treatment plan depends on this stage, and successful treatment will also affect survival. The conclusion of the biopsy in this case was poorly differentiated squamous cell carcinoma. OSCC is microscopically classified based on methods that consider subjective assessment, nucleus and cellular pleomorphism, degree of keratinisation, and mitotic activity. The grades include well-differentiated (grade I-II), moderately differentiated (grade III), and poorly differentiated (grade IV). Well and moderately differentiated tumours can be classified as low grade, while poorly differentiated tumours are classified as high grade.[18]

In a study conducted by Chin-Lin,[19] it was found that compared to OSCC grades I and II, grades III and IV were primarily found in younger patients, with locations predominantly on the front two-thirds of the tongue and partly in the back third. Patients with OSCC grade III and IV tumours showed poor survival and a higher risk of recurrence compared to other groups.[19] This patient may have been in grade III or IV when diagnosed. Tongue hemisection and chemotherapy are the treatment modalities that can be selected in poorly differentiated OSCC cases.

CONCLUSION

OSCC does occur in young women with a lack of known risk factors such as smoking, alcohol use and betel chewing. They should be promptly diagnosed and undergo further investigative tests, such as biopsy of the suspect lesion. Lifestyle, oral hygiene, and passive exposure to cigarette smoke may also be triggers, as identified in this patient. Improvement of the condition of the initial treatment should not deviate or delay the patient to proceed for the appropriate treatment of oral cancer.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this case report.

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