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ORAL LEUKOPLAKIA, THE FIRST CLINICAL FINDING OF ORAL SQUAMOUS CELL CARCINOMA (OSCC): A CASE REPORT

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ABSTRACT
Background*: Oral squamous cell carcinoma (OSCC) is preceded by oral potentially malignant disorders (OPMD). Oral leukoplakia (OL) is a non-scrapable white plaque lesion on oral mucosa and one of OPMD. Lack of knowledge about signs and symptoms of OPMD and health care providers are responsible for delays in establishing the diagnosis.* ***Objectives:*** *to improve health care provider's knowledge and the importance of detecting leukoplakia as an early sign of malignancy.* ***Case:*** *A 30-year-old woman came to the oral disease clinic at Hasan Sadikin Hospital complaining of canker sores and a lump on right tongue that had not been healed since 3 months ago. She had history of chronic irritation on tongue which was bitten by linguoversion tooth 46. Intraorally there was a solid mass, irregular edge in lateral right tongue at region tooth 46, 1.5 x 0.5 cm in size and a white plaque at region 46-48, 11 x 10 mm in size, could not be scrapped, unpainful on touched but felt sore when eating and drinking. Based on anamnesis, extraoral and intraoral examination, the working diagnosis was suspected fibroma region 46 and OL region 46-48.* ***Case management:*** *Pharmacological manage,ment was povidone-iodine mouthwash and referred to Oral Surgery Department. Well-differentiated OSCC was made as definitive diagnosis, based on histopathological examination and CT-Scan which showed bilateral lymph nodes enlargement. The patient was referred to Haemato-oncology Department for chemotherapy.* ***Conclusion:*** *it is important to do histopathological examination and CT-Scan as an effort for establishing OL as the early sign of malignancy.*

Keywords : *Oral cancer, Oral leukoplakia, Oral potentially malignant disorders*

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INTRODUCTION

One of the cancers found in the oral cavity is *Oral Squamous Cell Carcinoma* (OSCC). OSCC is a malignant neoplasm originating from the stratified squamous mucosal epithelium. Among all cancer cases, the incidence of OSCC is 2% - 4% with a mortality rate of about 250,000 worldwide each year and constitutes 90% of all oral malignancies which are the most commonly found from the head and neck SCC.[1,2] The most common prevalence of OSCC is the tongue (lateral), gingiva, buccal mucosa, floor of the mouth, and lips. Most patients with OSCC are diagnosed at an advanced stage with poor treatment and have poor survival. The cause of OSCC is still uncertain, but there are many factors that can influence the occurrence of OSCC, including the use of alcohol, tobacco, chronic irritation, unhealthy diet, hormones, viral infections, and genetics. [1,2,3,4,5]

Dentists pay special attention to OSCC due to the poor prognosis rate, patients only have a survival rate of ± 5 years from diagnosis to death with a mortality rate of around 50-55%. Early diagnosis is an important step to reduce cancer mortality. Nowadays, there is no organized program for screening and secondary prevention of OSCC in most parts of the world due to limited knowledge regarding the history of precancerous lesions and the clinical management of precancerous patients.[5,6,7] OSCC is preceded by precancerous lesions that are clinically established based on visual examination such as leukoplakia (white patches in the mouth), erythroplakia (red patches) and oral submucosal fibrosis (irreversible fibrosis of the submucosal tissue) and histopathologically there is dysplasia.[8,9,10,11]

Leukoplakia derived from Greek Language; *Leucos* means white and *placos* means plaque, therefore leukoplakia is often referred to as white plaque. Since several decades ago, the term *oral leukoplakia* (OL) was used to describe white plaque in the oral cavity that cannot be removed, with an incidence of about 0.4-2.6% of the world's population.[8] The etiology of leukoplakia

is not known for sure, but it can be triggered by many factors such as smoking, fungal, viral, and bacterial infections.[8,9,10,12,13]

OL is classified as *Oral Potentially Malignant Disorder* (OPMD), along with various oral lesions and conditions such as oral *lichen planus*, and erythroplakia, which initiated by the occurrence of epithelial dysplasia as a change towards malignancy to *oral squamous cell carcinoma* (OSCC). The rate of dysplastic change or malignancy in OL varied between 15.6% - 39.2%. OSCC and usually preceded by leukoplakia for about 5 years. Several other studies have shown that patients with OL have a 50-100 times greater risk for developing cancer than normal individuals. Clinically, OL with red lesions, although rare, has also been shown to have a higher risk of malignancy. [7,8,9,10]

The use of histopathological criteria to assess the degree of oral epithelial dysplasia through biopsy is a useful main indicator to determine the risk of malignancy change, although not all epithelial dysplasia of the oral mucosa develops into OSCC.[14] *Oral leukoplakia* can turn into OSCC, with a survival rate of about 80% in stages I and II, and 20% in stages III and IV.[15]It is important to prevent and detect malignancy changes in patients diagnosed with OL. This case report aimed to inform the importance of detecting OL as OPMD so that early detection of changes to malignancy could be carried out, especially in the pre-malignant stage, and is useful for getting a better prognosis so that OPMD morbidity and mortality can be reduced.[15]

CASE

A 30 years old woman, came to the oral disease clinic at Hasan Sadikin Hospital complaining of canker sores and lumps on the right lower tongue which never healed since 3 months before. The patient had a history of chronic irritation on the tongue because it was frequently bitten by linguoversion tooth 46. Intraoral examination revealed a solid mass, irregular border on the right lateral surface of the tongue at region 46, ± 1.5 x 0.5 cm in size, and there was a white plaque at region teeth 46-48, ± 1,1 x 1,0 cm in size which could not be scraped off, no pain on touched but felt sore when eating and drinking. (Figure 1). Based on the history, extra-oral and intra-oral examination, the clinical diagnosis was suspected fibroma at region 46 and oral leukoplakia at region 46-48.

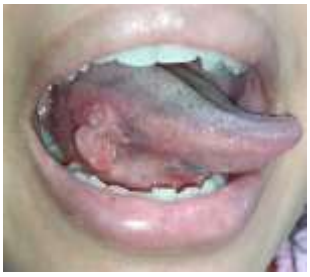

Figure 1. At the first visit, a polypoid mass, irregular border on the right lateral surface of the tongue at region tooth 46, ± 1.5 x 0.5cm in size, and a white plaque at region 46-48, ± 1,1x 1,0 cm that cannot be scraped off
(Source : personal documentation)

CASE MANAGEMENT

At the first visit , the pharmacological treatment for this patient was gargling with povidone-iodine mouthwash, 3 times a day. She was referred to the Oral Surgery Department for a biopsy. Laboratory and imaging investigations had been carried out, including histopathological examination and CT Scan as an effort to establish a definitive diagnosis in order to eliminate the possibility of malignancy. The oral surgeon was doing an incisional biopsy on the right lateral surface of the tongue around the region of tooth 46.

At the second visit, management of this patient was done by an oral surgeon including right hemiglosectomy, level I-IIA lymphadenectomy, and extraction of tooth 47. Then she was referred to the Hemato-oncology division for chemotherapy. There was also an enlargement of Colli dextra lymph nodes starting from level I, 2 x 1 x 1 cm in size. Based on the result of histopathological examination, well-differentiated OSCC with level III Colli bilateral lymphadenopathy was the definitive diagnosis.

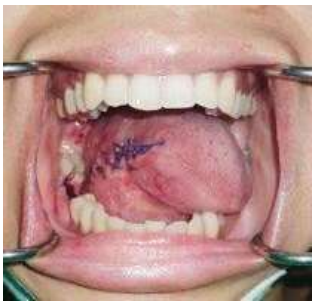

Figure 2. At the second visit, tongue condition after hemiglosectomy (Source : personal documentation)

DISCUSSION

OSCC is preceded by precancerous lesions that develop into a malignancy. Clinically the diagnosis is made based on visual examination such as leukoplakia (white patches in the mouth), erythroplakia (red patches) and

oral submucosal fibrosis (irreversible fibrosis of the submucosal tissue), and the presence of dysplasia histopathologically.[8,9,10,11]

The term “Potentially Malignant Disorders” was first introduced in 2005 at a workshop held by WHO in London. This meeting replaced the terms such as pre-cancer and pre-malignant to "Potentially Malignant Disorders" (OPMD) which are grouped into two, namely precancerous lesions and precancerous conditions. Precancerous lesions are morphological tissue changes in which oral cancers are more likely to occur such as leukoplakia and erythroplakia, whereas precancerous conditions refer to general conditions associated with a significantly increased risk of cancer such as lichen planus, discoid lupus erythematosus, and actinic keratoses.[8,9] According to the WHO definition, leukoplakia is a white patch or plaque that cannot be characterized clinically or pathologically as any other disease. In this case report, there was a white plaque at region teeth 46 - 48 that cannot be scraped off, did not pain on touch but felt sore when eating or drinking. Based on history, physical and intraoral examination, the clinical/working diagnosis for this white patch was suspected oral leukoplakia.

OL is one of the OPMD with many risk factors including smoking, alcohol consumption, chronic irritation, fungal, bacterial, and viral infections, malnutrition, hormonal disorders as well as ultraviolet exposure. The change towards malignancy from OPMD begins with the occurrence of chronic inflammation and is followed by epithelial dysplasia. The severity of dysplasia is thought to influence the development of malignancy.[8,9] Although less information is available regarding the definite prevalence of OPMD in the general population, it has been reported that the prevalence is 1-5% with the mean age of patients with OPMD being 50-69 years which is 5 years before the onset of oral cancer. In recent years, 5% of OPMD has been observed in people under the age of 30 years. The position of tooth 46 that linguoversion in this case, causing chronic irritation due to continuous friction on the right lateral surface of the tongue which resulted in the formation of granulation tissue which was suspected to trigger the occurrence of OL and fibroma that did not heal even though the tooth 46 had been extracted. Several factors that explain the risk of developing these lesions, such as the low levels of lateral and ventral protection of the tongue because they are thin and non-keratinized, rich in lymphatic tissues, and vascularity so that if there is continuous chronic inflammation in the area, it will easily lead to OSCC. [12,13,16,17]

Clinically, OL is classified into 2, namely homogeneous and non-homogeneous leukoplakia. The differences are based on the surface color and morphology of the lesions, especially the characteristics of thickness and texture. The homogeneous type is presented as a thin asymptomatic white plaque with a lower risk of turning into malignancy. Non-homogenous leukoplakia, presented as a thick white plaque, that are pain or painless varies in shapes such as granular (specked); nodules (nodular) in which there are small, round with red or white polypoid growths; verrucous (verrucous/wrinkled/corrugated) with an uneven wrinkled shape. [14,18,19] Based on the OL classification and clinical presentation of this patient, the clinical diagnosis was suspected non-homogeneous OL because it appeared as a white plaque with a few granules in the plaque area, cannot be scraped off, and asymptomatic with the formation of an exophytic polypoid mass.

Biopsy is the main standard in diagnosing leukoplakia to look for the presence or absence of epithelial dysplasia or even squamous cell carcinoma.[20] Other supporting examinations including CT scan was done to see enlarged lymph nodes, as well as to determine the clinical stage based on tumor expansion, regional lymph node metastases, and the spread of metastases.[21] In this patient, a biopsy on the right lateral surface of the tongue was done and the histopathological examination showed a stratified squamous epithelium which in one part had been transformed into a tumor mass. The tumor mass consisted of round, oval to polygonal cells that grow hyperplastic, condensed, and clustered. The nuclei of the cells are pleomorphic, hyperchromatic, and mitotic. The connective tissue stroma was filled with lymphocytic inflammatory cells with dilated blood vessels. There was also an enlargement of Colli dextra lymph nodes starting from level I, 2 x 1 x 1 cm in size (Figure 3). Lymph nodes were within the anterior m.digastric border, m. Stylohyoid, and mandible. Level 1 has a risk of malignant metastases from the oral cavity, anterior nasal cavity, facial soft tissue, and submandibular gland. [22,23]

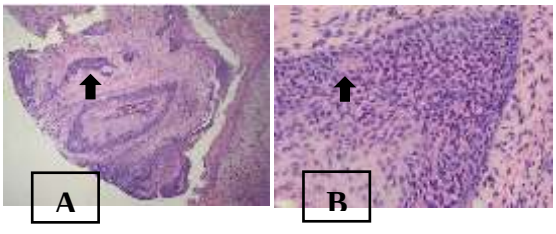

Figure 3. (A) Stratified squamous epithelium that partially had been transformed into a tumor mass
(B) Formation of a keratin mass. (Source : Anatomical Phatology Department, Unpad)

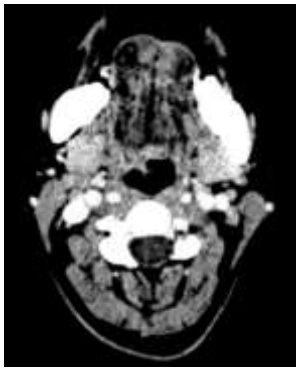

Figure 4. Multiple inhomogeneous isodense lesions, well-defined, regular edges, level II A, II B, III in bilateral colli. (Source : Anatomical Phatology Department, Unpad)

The definitive diagnosis of OL was confirmed by biopsy and CT scan. Two important parameters that must be considered in evaluating the potential change to malignancy of OL are: first, if there is a white lesion with and or without a red lesion, it should always be suspected as an OPMD and to confirm the findings of the lesion is by histopathological examination as soon as possible.[21] The second is to find out the enlargement of lymph nodes through a CT scan. In this patient, histopathological examination and CT scan biopsy had been carried out.

The conclusion is most cancers and their complications can be prevented through early detection by conducting histopathological examination and CT scan as an effort to establish the diagnosis of Oral Leukoplakia, to detect it as an early sign of malignancy.

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