

Early detection and treatment of Speckled leukoplakia

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ABSTRACT

Background: Leukoplakia is one of potentially malignant disorders that can be found on oral mucosa. Speckled leukoplakia is a rare type of leukoplakia with a very high risk of premalignant growth. Approximately 3 % of worldwide population has suffered from leukoplakia, 5-25% of which tend to be malignant leukoplakia. **Purpose:** This case report was aimed to discuss about early detection of speckled leukoplakia as one of potentially malignant disorders. **Case:** A 62 year old male patient came with chief complaint of bald and painful tongue since one month ago. The patient has a history of allergic reaction, hypertension, uric acid, and hepatitis B. He had been a heavy smoker since young until 10 years ago. Intra oral examination showed a firm, rough, non scrapable white plaque lesion with a size of 1 x 1.5 cm, surrounded by painful erosion with diffuse boundary. **Case Management:** Based on cytology examination, the patient was referred to oncologist to get an excisional biopsy. Next, the patient successfully underwent the excisional biopsy and came for control. The results showed the healing process of the lesion with a minimal complaint of bald tongue, especially when eating spicy or hot meal. To improve healing process, the patient then was given an antibacterial mouth rinse containing zinc and multivitamin. **Conclusion:** Speckled leukoplakia could show high malignant transformation rate, therefore, early detection and treatment are necessary.

Keywords: potentially malignant disorder; speckled leukoplakia; early detection

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INTRODUCTION

Public awareness of lesions that can potentially be a malignancy in oral cavity has been increasing. One lesion that can be found in the oral cavity is leukoplakia. Leukoplakia is derived from the word “leuko” which means white, and “plakia” which refers to the word plaques or patches. Thus, leukoplakia can be defined as a white plaque that cannot be scraped off. Its etiology, however, is still questionable after eliminating all risk factors that do not have a tendency toward malignancy.^{1,2,3} Approximately, 3% of the worldwide population has suffered from leukoplakia, 5-25% of which are pre-malignant lesions. After verified through histopathological examination, all lesions of leukoplakia can be considered as a potentially malignant lesion.³

One of leukoplakia types on oral mucosa is speckled leukoplakia or erythroleukoplakia, a non-homogeneous type. Speckled leukoplakia (SL) according to WHO, is a leukoplakia with a mix of white and red plaque lesions.^{2,4} SL is a form of leukoplakia that is rarely found with very aggressive high risk for transformation into malignancy, and also considered as precursor lesion for squamous cell carcinoma.⁴

Early diagnosis of SL can be based on clinical conditions in which there are white plaques with unknown etiology. If there is a local trauma, such as a tooth or sharp restoration, then the trauma factor should be eliminated. If within two weeks of healing it does not happen again, then the tissue biopsy should be done to eliminate the possibility

of malignancy.² Therefore, early detection and treatment of potentially malignant lesions in the oral cavity are important as a precautionary measure for the development of squamous cell carcinoma lesions.

CASE

A male patient aged 62 years came to the Oral and Dental Hospital of Faculty of Dental Medicine, Universitas Airlangga on October 27, 2014 on the referral of a private hospital in Surabaya with complaints of pain and thickening of the bottom left of the tongue. His tongue had felt bald and stinging since one month ago if exposed to spicy foods. There was also a wound near the thickened area that could bleed easily when touched. The tooth on the area near the tongue thickened was patched with black dental filling material two years ago. Before the tooth was patched, there was no complaint about the tongue.

The patient also has a history of allergy to the cold, high blood pressure, gout and high cholesterol, as well as hepatitis B. Therefore, he had regularly taken high blood pressure medicines, especially calcium antagonist class (amlodipine or nifedipine). In addition, he had also regularly consumed herbal drinks, such as turmeric and ginger solution. He had been smoking since the age of approximately 20 years, but he has stopped the habit since 10 years ago. There is a genetic predisposition in which his brother suffers from mammary carcinoma and bladder carcinoma.

Based on submandibular gland examination, his left submandibular gland was palpable, soft, supple, and pain. On the left ventral tongue (Figure 1), there was a single, oval, white plaque lesion sized 1 x 1.5 cm that could not be scraped with rough surface, regular edges, clear boundaries, and pain. In addition, there were also two oval-shaped ulcers sized 2 x 3 mm and 7 x 3 mm with redness color, pseudomembranous coated surface, regular edges with diffuse boundaries, easy bleeding, and pain. On tooth 37,

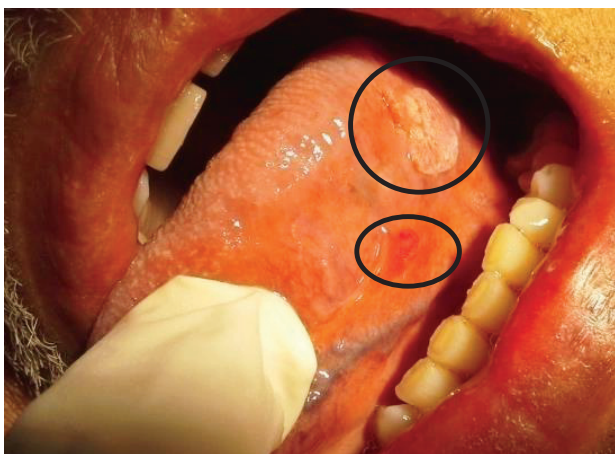


Figure 1. There was a single white lesion and two ulcers on the ventral surface of the tongue.

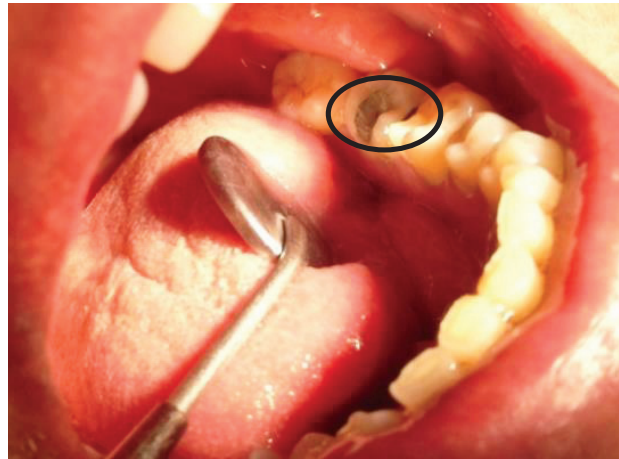


Figure 2. There was an amalgam filling on tooth 37 with a sharp edge.

there was amalgam filling with sharp edges.

CASE MANAGEMENT

Based on the history and the extra-oral and intra-oral clinical examination, a temporary diagnosis of leukoplakia was set with a diagnosis of traumatic keratosis. The patient then was instructed to perform a complete blood count and liver function (SGOT/SGPT) test. He was also referred to the Conservative Dentistry to improve his sharp tooth filling. As symptomatic and supportive therapy, the patient then was given topical steroid anti-inflammatory drugs (triamcinolone acetonide in ora base 0.1%) three times a day, applied at the lesion. The patient was also advised to avoid the consumption of spicy food, and come back after the filling was improved and the laboratory results were received.

In the second visit, the patient denounced the recommended laboratory tests, and went to Dr. Ramelan Navy Hospital Surabaya to seek another opinion on his own initiative. His dental filling still was not repaired.

In Dr. Ramelan Navy Hospital, cytology biopsy examination was performed with *scraping* on the lesion. The results of the histopathological examination showed squamous epithelial cell dysplasia, from mild to moderate, and also atypical cells. Thus, the patient was advised to undertake an excisional biopsy, but the patient refused. The patient was then educated to follow the advice to perform an excisional biopsy as the results of the histopathological examination, but the patient still was not willing.

In the third visit, three months later, the patient came with complaints of pain in the tongue getting worse, difficulty of swallowing, and pain terraces up to the neck. On the examination of submandibular gland, moreover, the left submandibular gland was palpable, chewy, pain, and static. Based on the results of the intra-oral examination,

there was a single white oval plaque lesion sized 1 x 1.5 cm with clear boundaries, regular edges, and rough surfaces on the left lateral tongue, that could not be scraped and caused pain. There was also a redness erosion emerged on the area around the plaque extending to the base of the tongue with diffuse boundaries and pain (Figure 3). The dental filling was then replaced with composite materials. Finally, the patient was willing to be referred to an oncologist to perform the excisional biopsy in Dr. Ramelan Navy Hospital.

Excisional biopsy surgery was conducted on February 11, 2015 by an oncologist. The results of histopathological examination showed leukoplakia with mild dysplasia. Two months after the surgery, the patient began to feel comfortable, but his tongue still felt bald when exposed to hot or spicy food. During the intra-oral examination, a single erosion sized 5 x 3 cm with irregular edges, diffuse boundaries, and painless was found (Figure 4). This condition can be considered as the healing process of the excisional biopsy surgery. The patient was prescribed with antibacterial mouthwash, made of sodium chlorite, *aloe vera*, and zinc three times a day, as well as vitamin supplements (B complex, vitamin E, vitamin C, and *zinc*) once a day. The patient was also advised to avoid spicy and hot food/beverage.

Six months after the surgery, the patient still felt pain in tongue when exposed to spicy or fried food. Tongue and left cheek were often bitten, causing injuries. Intraoral examination of the left lateral tongue showed macular erythematous with diffuse boundaries no pain, and no nodule or induration found on the palpation (Figure 5). On the left buccal region of the right upper second molar (27), there was a single ulcer with irregular edges, clear boundaries, and pain. The occlusal surface of the premolars, (34 and 35) and the left mandibular second molar (37) and left upper jaw (27) was noticeably sharper. Examination using Velscope® was also conducted on the entire mucosal surface, and the results did not reveal any areas that absorbed light (dark).

To reduce the risk of trauma to the buccal and lateral tongue, *occlusal grinding* was performed on the surface of the teeth 34, 35, and 27. For traumatic ulcer, a treatment was conducted by applying topical steroid anti-inflammatory drugs (triamcinolone acetonide in ora base 0.1%). The patient was also educated to increase the consumption of fruits and vegetables containing high beta-carotene, such as tomatoes and carrots, as well as to avoid spicy and fried food. Based on the results of the clinical features and the final diagnosis of the histopathological examination, it was diagnosed as speckled leukoplakia.



Figure 3. The widespread of erosion on the tongue (on visit 3).



Figure 5. The wound healing process after the excisional biopsy with erythematous macular on the left lateral surface of the tongue.



Figure 4. The condition of the patient's tongue two months after the excisional biopsy surgery.

DISCUSSION

During the first examination, the patient was diagnosed with leukoplakia with traumatic keratosis diagnosis based on clinical description in which there are white nodular lesions and dental filling using amalgam materials with sharp edges. But after the dental filling was repaired, in the next two month control, the lesion was not improved, but getting worse by erosion around the nodular lesion. The patient was then referred to the oncology department for further examination and treatment. This is in accordance that if local factors have been eliminated and there is no improvement in the lesion, the patient should be referred for biopsy examination.²

SL diagnosis can be made on clinical and histopathologic examinations. SL is a type of non-homogeneous leukoplakia with the clinical picture in the form of plaques, nodular, or white granular with reddish basis.^{2,5,6} SL is often accompanied by pain and discomfort^{4,7} as perceived by the patient.

Leukoplakia is primarily a clinical term. Histopathological findings of the biopsy consists of surface epithelial hyperplasia and hyperkeratosis, atrophy with or without dysplasia cells. Dysplasia cells can be mild, moderate, or severe.^{2,7} Epithelial dysplasia is commonly found in homogeneous leukoplakia, but less in non-homogeneous leukoplakia.² The results of histopathological examination after the excisional biopsy in the patient showed hyperkeratosis epithelium, mild dysplasia, and intact basement membrane.

Predisposing factors of SL in this case were old smoking habit (\pm 30 years) and chronic trauma of sharp dental filling edge. Tobacco in various forms is the primary etiology of leukoplakia, especially tar contained in tobacco considered as toxics and carcinogens. Furthermore, mechanical trauma is also considered as a factor that plays a role in the pathogenesis of leukoplakia.⁷ Based on animal studies, chronic trauma accompanied by the risk factors and carcinogenic materials (such as tar) will trigger epithelial cell transformation.⁸

Therapy for SL is an aggressive surgery, excisional biopsy. In addition, the elimination of risk factors (smoking and alcohol consumption) and etiological factors (sharp teeth, metallic restorations, and dentures bridges that do not fit) can be a precaution that can be conducted.⁴ Control regularly every three months in the first year is also recommended. If the lesions are not recurrent or there is no change in the mucosa, so the control time can be increased to six months. If there is a change in the mucosa, biopsy should be performed again. If after five years, there is no change in the mucosa, patients are advised to observe themselves.^{2,8} For the patient in this case, the excisional biopsy therapy was chosen based on the results of the initial cytologic examination showing mild to moderate dysplasia cells in the presence of atypical cells. Similarly, surgical

therapy, is chosen based on the discovery of the epithelial cells that undergo dysplasia.⁷

Symptomatic therapy given to the patient, was an antibacterial mouthwash made of sodium chlorite, aloe vera, zinc, and vitamin B complex supplements plus zinc. The antibacterial mouthwash was given to improve the oral hygiene of the patient. Sodium chlorite, aloe vera, and zinc contained are expected to help the healing process of the tissue. Sodium chlorite will produce oxygen, which is essential for cell metabolism, specifically the production of energy via adenosine triphosphate (ATP). Oxygen can prevent infection in wounds, stimulate angiogenesis, increase differentiation, migration as well as keratinocytes re-epithelialization, increase fibroblast proliferation and collagen synthesis, and trigger wound contraction.

In addition, level of superoxide production by polymorphonuclear leukocytes, necessary to kill bacteria is highly dependent on the level of oxygen.¹⁰ The administration of zinc is also expected to enhance the regeneration of the epithelial cells since zinc can activate transforming growth factor beta (TGF β), which plays a role in the early wound healing process.¹¹ Zinc may also play a role in the activation of metalloproteinase enzymes that play a role in the process of collagenase.¹² The administration of multivitamin containing vitamin B complex, vitamin E and vitamin C, and zinc, moreover, aims to help the wound heal process. Vitamins E and C have antioxidant and anti-inflammatory effects on the wound healing process.¹⁰ Vitamin B complex plays a role as co-enzymes that catalyze biochemical reactions in body.¹³

There are several factors triggering malignant leukoplakia.^{4,7,14} First, age factor can make the elderly people increasingly at risk. Second, size factor of lesions can trigger the risk if it is larger than 2 cm. Third, habits factor can lead to the risk of malignancies, especially more common in smokers than non-smokers. Fourth, the location of the lesions on the tongue and floor of the mouth is more at risk than the buccal mucosa and commissure. Fifth, sex factor can also trigger the risk, which means women have higher risk of malignancies than men do. Sixth, clinical types can lead to the risk more than non-homogeneous type. Seventh, epithelial dysplasia can be considered to have a higher risk for experiencing malignancies. Eight, leukoplakia accompanied with candidiasis infection can trigger more the risk of malignancies. Ninth, the presence of ulcers, erosions, or nodules can also trigger the risk. This patient had six of the nine factors that influence the malignant tendencies of SL suffered. Therefore, early detection and excisional biopsy are essential to prevent potential malignancy of the lesion

Nowadays, a tool to detect epithelial dysplasia has been developed and set in dental chair. *Velscope*® (visually enhanced lesion scope) is a tool that does not require dye and needs shorter examination time. This tool is based on

the principle that normal cells will glow when exposed to fluorescent light, while abnormal cells will absorb the fluorescent light and be looked dark.¹⁵ This tool, can assist dentists in detecting the early presence of an abnormality in oral mucosa so that prevention from the malignant transformation can be performed early. The results of the examination using Velscope® during visits six months after the excisional biopsy did not reveal any areas that absorb light (dark). It means that there were no cells suffering from dysplasia. Therefore, there was no sign of malignancy.

In conclusion, leukoplakia, especially SL, is a lesion that can lead to high malignancy, especially if there is epithelial cell dysplasia. Dentists play an important role in early detection of suspicious lesions leading to malignancy, which then could affect the prognosis for patients. In other words, early detection and treatment of lesions are important to prevent the possibility of lesion transformation into a malignant lesion.

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