

Case Report

Oral leukoplakia associated with amalgam restorationsZeynep B. Gönen^{1,2}, Canay Yılmaz Asan¹, Osman Etöz¹, and Alper Alkan¹¹Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Erciyes University, Kayseri, Turkey²Genome and Stem Cell Center, Erciyes University, Kayseri, Turkey

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Abstract: The World Health Organization has defined oral leukoplakia (OL) as “a white patch or plaque of the oral mucosa that cannot be characterized clinically or pathologically as any other disease”. A 21-year-old male with OL presented with a bilateral burning sensation in the buccal mucosa. The patient had amalgam restorations, and an epicutaneous patch test indicated a positive response to amalgam. The amalgam restorations were therefore removed and the cavities were refilled with a composite resin restorative material. During 5 years of follow-up, there was no recurrence of the oral lesions. This case illustrates that amalgam fillings may cause OL lesions. (J Oral Sci 58, 445-448, 2016)

Keywords: oral leukoplakia; amalgam; premalignant lesion.

Introduction

Oral leukoplakia (OL) is defined by the World Health Organization as “a white patch or plaque of the oral mucosa that cannot be characterized clinically or pathologically as any other disease” (1). The prevalence of OL ranges from 0.5 to 3.4% with a peak incidence rate in individuals older than 50 years. According to the literature, most oral carcinoma cases are associated with, or preceded by, clinically detectable premalignant lesions such as OL. The malignant transformation rate of OL is reported to be in the range of 0.1 to 17% (2).

The etiological factors most commonly associated with OL have been smoking, alcohol abuse, candidiasis, HPV infection, iron deficiency, and low serum levels of vitamin A and beta-carotene (3). Zinsser-Cole Engman syndrome, a genodermatosis commonly known as dyskeratosis congenita, includes oral manifestations such as OL. Many different non-surgical and surgical modalities such as conventional surgery, electrocauterization, laser ablation, cryosurgery, and medications such as vitamin A, vitamin B, and bleomycin, have been reported for treatment of OL (4).

Dental amalgams remain the most commonly used posterior restorative material in dental practice. A relationship has been established between contact allergy to mercury and oral lichen planus (5). Although amalgam-related conditions such as burning mouth, xerostomia, and musculoskeletal and neuropsychological symptoms have been reported, the relationship between amalgam and OL has not yet been examined.

This report documents a patient with OL lesions who showed a positive skin patch test reaction to amalgam and who subsequently recovered after his amalgam restorations had been removed and replaced with a different material.

Case Report

A 21-year-old male was referred to the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Erciyes University, with suspected OL. His major complaint was a bilateral burning sensation in the buccal mucosa. The patient had previously received cryotherapy and laser treatment at a dermatology clinic, but the OL lesions had not healed. Intraoral examination revealed white lesions bilaterally affecting the buccal mucosa and tongue (Figs. 1-3). The patient had no systemic disease and no history of tobacco or alcohol consumption. In order to confirm the histological nature of the lesion, an incisional biopsy

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of the left buccal mucosa was performed. The histopathological findings were compatible with a clinical diagnosis of OL.

Topical corticosteroid treatment (Kenacort A-orobase, Deva, Istanbul, Turkey) was applied for 6 weeks. As the condition did not improve, systemic corticosteroid treatment was administered after consultation with the dermatology department. However, this treatment was ineffective.

The right second molar had a bucco-occlusal amalgam filling, and the left mandibular molar and right upper molar had occlusal amalgam fillings. The amalgam restorations were not defective, the surfaces were well adapted, and the restorations had been placed about 1 year previously. A detailed examination of the patient's medical history revealed that the onset of the OL lesions had coincided with the times of dental treatment. The OL lesions had persisted since the patient's first visit, and there was no sign of any resolution or difference in their appearance. It was suspected that the patient had developed hypersensitivity reactions to the amalgam or its components. An epicutaneous patch test was therefore performed at our dermatology clinic to determine whether such sensitivity might be contributing to the persistence of the lesions. A patch soaked to a 0.05% mercuric chloride solution was attached to the medial aspect of the patient's right arm, and after 48 h the skin was observed for any reaction such as erythema or effusion. The patch test indicated a positive response. Therefore, the amalgam restorations were removed and the cavities were refilled with a composite resin restorative material. In the 3 weeks following removal of the amalgam, the lesions were completely resolved. We then followed up the patient to confirm that the lesions had been due solely to the amalgam restorations. During a follow-up period of 5 years, there has been no recurrence of the oral lesions (Figs. 4-6).

Discussion

Oral leukoplakia has been found to be associated with tobacco use and alcohol consumption. It has also been reported that the risk of developing OL is greater in smokers than in non-smokers (6). Generally, individuals who smoke also consume alcohol. Although alcohol alone has not been associated with development of leukoplakia, it may act synergistically with tobacco to promote the development of leukoplakia and oral cancer (3). Mechanical trauma such as chronic cheek biting may also be a contributory factor for OL. Sanguinaria, a herbal extract used in dental hygiene products such as toothpaste and mouthwashes, has also been found to be associated



Fig. 1 OL lesion of the right buccal mucosa before treatment.

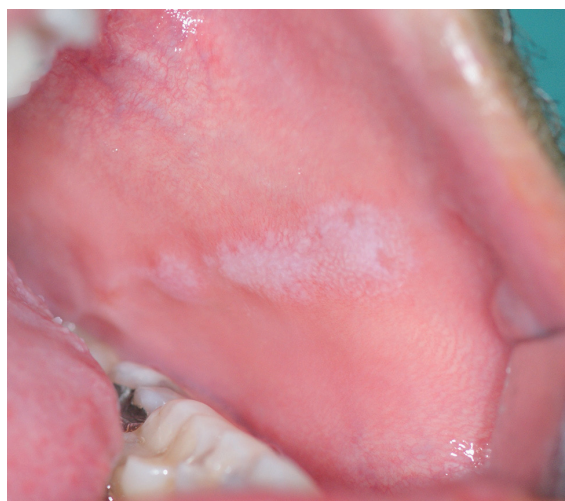


Fig. 2 OL lesion of the left buccal mucosa and an amalgam restoration in the lower mandibular tooth before treatment.

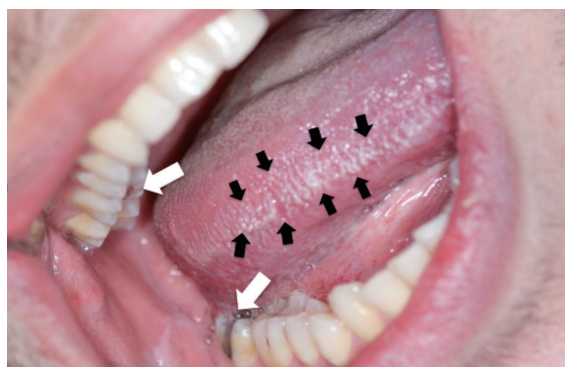


Fig. 3 OL lesion on the right lateral aspect of the tongue before treatment. Black arrows indicate the lesion and white arrows indicate the amalgam fillings in the upper and lower molars.

with development of OL. Some microbiological studies have focused on fungal and viral agents (*Candida*, HPV, EBV) as etiological factors associated with OL development (6,7). Our present case suggested that amalgam



Fig. 4 Resolution of the OL lesion on the right buccal mucosa after removal of the amalgam restorations. Arrows show the composite resin fillings.



Fig. 5 Resolution of the OL lesion on the left buccal mucosa after removal of the amalgam restorations.



Fig. 6 Resolution of the OL lesion on the lateral aspect of the tongue.

restorations may also be an OL-related etiologic factor.

OL can also be regarded as a potentially premalignant disorder, and several factors may increase the risk of malignant transformation. It has been reported

that epithelial dysplasia is one of the most important indicators of potential malignancy (6). Generally, non-homogeneous lesions or pure erythroplakia have a higher risk than lesions with a homogenous appearance (8). Lesions on the tongue or floor of the mouth also have a higher potential for malignancy. Old patients have a much higher risk for transformation (1). The incidence of OL increases with age, and it has been estimated that fewer than 1% of affected men are less than 30 years old. As the present patient was 21 years old, his OL was considered to have arisen at an unusually young age.

It has been reported that epithelial dysplasia is the best predictor of malignant transformation of OL, but recent studies have shown that DNA ploidy, p53 gene expression, and markers such as podoplanin are parameters that also need to be studied in order to determine the transformation rate and prognosis of the lesions (7). Loss of heterozygosity (LOH) has been validated as a risk predictor for malignant transformation (6). Lesions with LOH at 3p and/or 9p have a greater risk of malignant transformation than those retaining heterozygosity at these loci. The mode of management chosen for OL has an important impact on transformation potential.

The first stage of management for oral lesions is the elimination of possible causative factors. For persistent lesions or in cases where possible related factors are not evident, incisional or punch biopsy is advisable. Incisional biopsy including some adjacent healthy tissue should be performed for large lesions, whereas excisional biopsy should be the choice for small lesions. Many different non-surgical and surgical modalities for OL have been reported, including conventional surgery, electrocauterization, laser ablation, or cryosurgery (6,7). Conventional surgery for OL may include excision of the lesion with or without use of a dressing material. Medications such as vitamin A, retinoids, beta-carotene, vitamin E, and bleomycin have a place in non-surgical treatment of OL (4). Although administration of retinoic acid or beta-carotene may be effective for resolution of OL, randomized controlled trials of non-surgical treatment have demonstrated no evidence of effectiveness for preventing malignant transformation or recurrence. The present patient had undergone non-surgical treatment (topical and systemic corticosteroid administration) and cryotherapy along with laser treatment, which has been shown to be a safe and effective approach for treatment of OL. However, complete resolution of the lesions was not achieved. Recurrence of OL after surgical treatment has been reported in more than 10% of cases (9). Etiological factors such as amalgam restorations may be a complicating factor in cases where lesions do not heal, or

which recur after surgical treatment. In the present case, during a follow-up period of five years after replacement of the amalgam restorations, no recurrence of the lesions was observed.

Dental amalgam remains the most commonly used posterior restorative material in dental practice. Several amalgam-related conditions such as burning mouth, xerostomia, and orofacial granulomatosis caused by hypersensitivity to amalgam have been reported. Mercury compounds may also cause musculoskeletal and neuropsychological symptoms (9). It has been proven that contact allergy to mercury is directly correlated with the incidence of oral lichen planus (5). The term 'oral lichenoid lesion' is commonly used to describe such lesions that develop as a consequence of dental restorations (1,5,9). The clinical appearances and histopathologic changes associated with oral lichenoid lesions and oral lichen planus are similar. The immunological basis for oral lichenoid lesions caused by restoration products is contact allergy or type IV hypersensitivity, which is known to be a manifestation of an excessive immune response to an antigen, leading to tissue damage. Whereas skin contact allergic reactions are common, such reactions in the oral mucosa are rare (2). Many authors claim that there is a connection between type IV allergy to mercury compounds released from dental amalgam and oral lichen planus (9). However, the underlying mechanism responsible for OL caused by amalgam remains unclear.

Previous studies have shown that if skin tests elicit a positive response, then the tested material should be removed from the oral cavity (10). It is commonly recommended that amalgam fillings should be removed, not only in cases of oral lichen planus but also in cases of OL where patch testing for amalgam yields a positive result. In the present case, the OL lesions healed soon after removal of the amalgam. Reports in the literature suggest that oral lesions associated with contact hypersensitivity, especially to dental metals, carry a possible risk for development of oral squamous cell carcinoma (5).

In conclusion, treatment of clinically detectable premalignant lesions is very important for prevention of oral carcinoma. The main objective in the management of OL is to detect and to prevent malignant transformation. The present case illustrates that the possibility of amalgam fillings leading to OL lesions should always be kept in

mind. If OL lesions prove resistant to conventional treatment modalities in patients with amalgam restorations, we recommend that patch testing should be performed, and if this indicates a reaction to mercury or components of amalgam, replacement of such restorations is advisable.

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