

Amalgam-Associated Oral Lichenoid Reactions: A Case Series

Aida KURBANOVA¹ , Gürkan ÜNSAL¹ , Kaan ORHAN^{2,3} 

ABSTRACT

Aim This case series report aims to discuss clinical findings of lichenoid reactions that were induced by amalgam fillings in 3 patients.

Case Report Three patients who applied to our clinic with the complaint of a burning sensation in the buccal mucosa were referred to our clinic. All patients were males who had amalgam restorations. Only one of the patients described a burning sensation in both the buccal mucosa and the lateral side of the tongue. In all three patients, intraoral examination revealed white lichenoid lesions which are located at the relevant complaint areas and were close to a large amalgam restoration that is in contact with the mucosa. The lesions were associated with amalgam fillings. One of the cases had a patch test regarding the dental materials and had a positive patch result to dental amalgam which is important in the oral lichenoid lesions diagnosis.

Discussion Two studies in the literature suggest a link between metal dental fillings and immunopathological lesions in the oral mucosa. Sensitization to mercury, found in amalgam fillings, is associated with oral lichenoid lesions. Corrosion of dental alloys is correlated with the development of lichenoid lesions. Dental amalgam can induce immunological reactions, including increased autoantibody production. Replacing amalgam fillings resulted in complete remission of lesions in patients without other metal restorations.

Conclusion Burning sensation in the buccal mucosa was common in 3 patients and this was the main complaint.

Keywords Amalgam filling, Autoimmunity, Mercury, Oral lichen planus, Oral lichenoid reactions

Introduction

Autoimmunity is the immune response to one's antigens. Although it plays a certain physiological role, a poorly regulated, exaggerated, and misdirected autoimmune response can lead to autoimmune diseases (AD), which are characterized by tissue/cell damage. AD represents a breakdown of self-recognition mechanisms (1). ADs are a heterogeneous group of diseases with common key links in pathogenesis and risk factors. Various environmental factors play an important role in the development of pathological autoimmunity, including infections, xenobiotics, vitamin D deficiency, ultraviolet radiation, stressors, and exposures that disrupt melatonin regulation. Such factors often have regular seasonal dynamics, which can affect the development of the disease, its severity, and its course (2). Adjuvant and adjuvant-like substances are widely used in dental practice for the manufacture of implants, prostheses, and fillings and can cause autoimmune reactions. Metals that are part of fillings are one of the main adjuvants - triggers of AD (3). Thus, in dentistry, for permanent restoration of teeth, mercury-free metal fillings and mercury copper and silver fillings of the I - III generations are used. Amalgam is an alloy of mercury (Hg) with one or more metals that melts at ambient temperatures. Amalgam takes on a characteristic crystallization, imparting certain properties to the filling when various metals are added to it. An

amalgam alloy can contain solid particles of silver (Ag), tin (Sn), copper (Cu), and sometimes zinc (Zn), palladium, indium, and selenium (4).

Mercury and autoimmunity

Several studies have examined the effects of various forms of Hg, including elemental (Hg), inorganic (IHg), and organic (OHg), and their relationship to autoimmunity. In vitro studies using peripheral blood mononuclear cells from healthy individuals have shown that methylmercury (MeHg) causes cell death at lower concentrations than IHg, although exposure to IHg leads to a stronger proinflammatory effect than MeHg. In vivo studies using mouse models susceptible to the development of induced autoimmune disorders have shown that exposure to IHg leads to the lupus-like syndrome, antinuclear and antifibrillin autoantibodies arise, and immunocomplex lupus nephritis is formed, while mice exposed to MeHg develop autoimmune reactions without an immunocomplex component (5). In addition, lower IgE concentrations are found in animals treated with MeHg compared to those treated with IHg. It turned out that OHg harms animal lines with a predisposition to autoimmune pathology (6).

Oral lichen planus (OLP)

Oral Lichen planus is a chronic disease accompanied by an inflammatory component and pathophysiologically manifested by hyperkeratosis (7), and clinically - by the presence of white striae on the oral mucosa (Wickham's striae), which appear in reticular, papular, atrophic, plaque-like, erosive or bullous forms (8).

Additionally, in the development of the disease as a whole and each specific case, separate concomitant factors are distinguished, which, most likely, also play a role in the pathogenesis of the disease. The most significant of them:

- OLP can often be triggered by drugs, such as methyldopa (9), beta-blockers (10), and antiphlogistics (11).

Correspondence: Aida KURBANOVA, aida.kurbanova@neu.edu.tr

¹ Near East University, Faculty of Dentistry, Department of Dentomaxillofacial Radiology, Nicosia, Cyprus

² Ankara University, Faculty of Dentistry, Department of Dentomaxillofacial, Ankara, Turkiye

³ Ankara University, Medical Design Application and Research Center (MEDI-TAM), Ankara, Turkiye

- The presence of any concomitant chronic disease of internal organs, in particular, the liver, gastrointestinal tract, and endocrine system (the symptom-complex syndrome of Grinshpan is described, along with OLP, in which diabetes mellitus and hypertensive disease).
- Local traumatic factors of mechanical, physicochemical, chemical, and biological origin, incl. the presence of amalgam fillings in the oral cavity (12).

Diagnosis of Amalgam induced Oral Lichenoid Reactions

Suspicion will be raised regarding the detection of an oral white lesion that is close to a dental amalgam filling. Idiopathic OLP, however, may also manifest in traumatized locations as a result of friction from abrasive restorative materials. Clinicians should also focus on the detection of any lesion that is localized at the lips, skin, nails, and scalp. In the presence of an amalgam-induced OLP, the histological results of the biopsy will be the same as an idiopathic OLP; thus, the clinical examination must be done thoroughly. The same as with idiopathic OLP, immunofluorescence may be used to rule out autoimmune disorders of the mouth. Patients with amalgam-induced OLPs are more likely to test positive for amalgam and inorganic mercury salts than those with idiopathic OLP. As even a negative patch test result will not eliminate the possibility of an amalgam-induced OLP the role of this test in making the diagnosis is not fully diagnostic yet. Biopsy type-independent, the outcomes of the tests cannot diagnose the induction of the amalgam filling for the OLP. The most diagnostically accurate method is to replace the amalgam filling with another restorative material, and routine follow-up of the patient (13-16).

Our study aimed to report cases of lichenoid reactions associated with amalgam, thus supporting the hypothesis that amalgam fillings can cause lichenoid reactions in the oral mucosa, and showing that there is sufficient reason for more comprehensive studies.

Case Report

Case #1: A 47-year-old male patient was referred to our clinic with a burning sensation which is localized at the right lateral border of the tongue and left buccal mucosa. Intraoral examination revealed white lichenoid lesions which are located at the complaint areas. The lesions were associated with amalgam fillings (Figure 1).

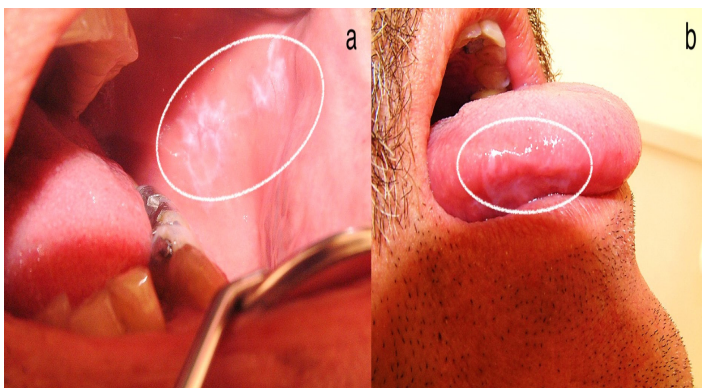


Figure 1: (a) Lichenoid lesion on the left cheek mucosa; (b) Lichenoid reaction due to amalgam filling on the right lateral side of the tongue.

Case #2: A 39-year-old male patient was referred to our clinic with a burning sensation which is localized at the left buccal mucosa. Intraoral examination revealed white lichenoid lesions which are found close to a large amalgam restoration. The patient had a patch test regarding the dental materials and had a positive patch result to dental amalgam which is important in the Oral Lichenoid Lesions diagnosis (Figure 2).

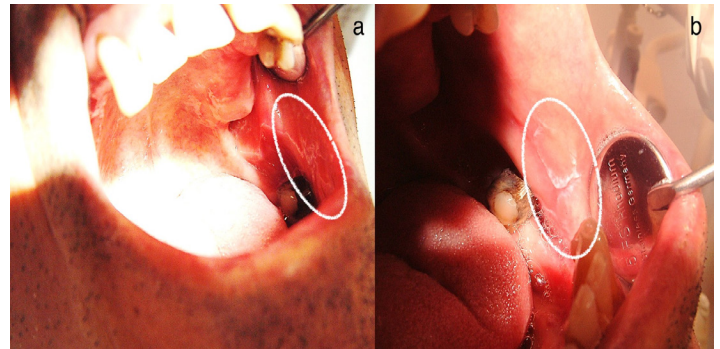


Figure 2: Lichenoid lesion on the left cheek mucosa; (a) Before the filling of tooth 37 is removed; (b) After amalgam filling has been replaced.

Case #3: A 20-year-old male patient was referred to our clinic with a burning sensation that is localized at the right buccal sulcus. Intraoral examination revealed a white lichenoid lesion which is found near the amalgam filling. (Figure 3).

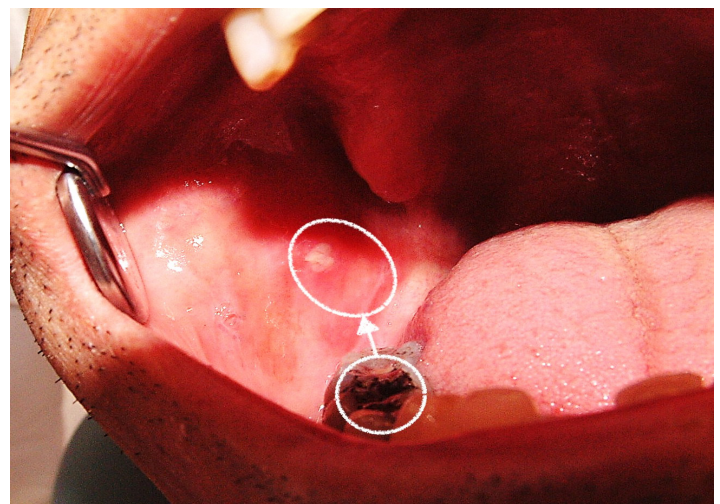


Figure 3: Lichenoid lesion on the right buccal sulcus.

All three of our patients had an autoimmune disease.

Discussion

A 1999 study (17) showed that the metals of dental fillings are associated with the development of immunopathological lesions of the oral mucosa, with Hg (as the main component of amalgam) considered as the main cause. In this study, the frequency of sensitization to metal salts was determined in 194 patients. At the same time, pathological studies of biopsy samples from carriers of positive tests for sensitization to metal salts were additionally carried out and the effect of amalgam removal was investigated to find out whether there would be an improvement from this procedure. The test was conducted using a standard range of dentures and a range of metal salts including gold, Hg, and palladium, as

well as other metals used in dental restorations. Sensitization to Hg has proven to be important, although perhaps not the only cause of oral lichenoid lesions.

In 2016, Romanian authors (18) published research data on the correlation between the corrosion restoration of dental alloys and the development of lichenoid lesions of the oral mucosa. They analyzed the corrosion processes occurring in metal stationary dental fillings in a group of patients with lichenoid lesions, along with their entire electrochemical characteristics. Lichen planus of the oral mucosa is considered a non-infectious chronic immunopathological disorder of unknown etiology that involves the oral mucosa. Similar lesions are typical for the onset of many autoimmune lesions of the oral cavity, in particular discoid lupus and pemphigus, and sometimes occur before neoplasia. The presence of metals in the oral cavity is considered a triggering factor for this form of pathology. The authors analyzed alloys restored after removing some old metal fillings in patients with lichenoid lesions. Their composition was determined using energy-dispersive X-ray spectroscopy. They also measured the electrochemical properties of these materials. Highly alloyed alloys and alloys based on chromium and nickel with different electrochemical behavior were studied. The results showed a correlation between the process of metal corrosion in the oral cavity and the development of lichenoid lesions.

In the literature, experimental and clinical data were published that dental amalgam can induce immunological reactions in genetically susceptible animals and humans. Thus, in genetically susceptible lines of experimental animals, Hg and Ag induce autoimmune reactions. The sera of Hg-sensitive patients were found to have higher autoantibody titers relative to controls. After in vitro stimulation of peripheral blood lymphocytes with HgCl₂, the presence of antinuclear SSB / La auto-antibodies was determined. Lymphocytes were obtained from patients with autoimmune thyroiditis and an increased immune response to mercury in vitro. Mononuclear cells were cultured for 6 days with 100 µl HgCl₂ solution or with pure medium, and the levels of SSB / La antinuclear autoantibodies were analyzed by enzyme immunoassay. Increased production of SSB / La auto-antibodies after stimulation of peripheral blood lymphocytes with HgCl₂ was detected in all cases. Thus, in patients with Hashimoto's thyroiditis and a dental filling with mercury, the production of antinuclear autoantibodies can be stimulated. Thus, it seems that IHg is associated with autoimmune pathology to a greater extent than OHg, although their effect on morbidity in the population is not yet fully understood (19, 20).

Allergy to filling materials may be one of the pathogenetic mechanisms since in all three patients, apart from amalgam fillings, there were no other metal restorations in the oral cavity and there was a complete remission of lesions after amalgam replacement.

Conclusion

Consistent with the works described above, the present report supports the hypothesis that amalgam restorations may be an etiological factor in lichenoid changes in the oral mucosa.

Declarations

Author Contributions: Conception/Design of Study- K.O.; Data Acquisition- A.K., G.Ü., K.O.; Data Analysis/Interpretation- A.K., G.Ü., K.O.; Drafting Manuscript- A.K.; Critical Revision of Manuscript- G.Ü., K.O.; Final Approval and Accountability- A.K., G.Ü., K.O.; Material and Technical Support- A.K., G.Ü., K.O.; Supervision- K.O.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

- Perricone C, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: Unveiling the pathogenic, clinical and diagnostic aspects. *J Autoimmun.* 2013;47:1-16.
- Watah A, Azrielant S, Bragazzi NL, Sharif K, David P, Katz I, et al. Seasonality and autoimmune diseases: The contribution of the four seasons to the mosaic of autoimmunity. *J Autoimmun.* 2017;82:13-30.
- Mignogna MD, Lo Muzio L, Lo Russo L, Fedele S, Ruoppo E, Bucci E. Clinical guidelines in early detection of oral squamous cell carcinoma arising in oral lichen planus: a 5-year experience. *Oral Oncol.* 2001;37(3):262-7.
- Eliaz N. Corrosion of Metallic Biomaterials: A Review. *Materials (Basel).* 2019;12(3).
- Dunsche A, Kastel I, Terheyden H, Springer IN, Christophers E, Brasch J. Oral lichenoid reactions associated with amalgam: improvement after amalgam removal. *Br J Dermatol.* 2003;148(1):70-6.
- Cruz-Dominguez MP, Vera-Lastra O, Deras-Quinones A, Jandete-Rivera F, Grajeda-Lopez P, Montes-Cortes DH, et al. Mercury tissue deposits: a new adjuvant in autoimmune/inflammatory syndrome. *Isr Med Assoc J.* 2013;15(11):716-9.
- Shklar G, Meyer I. The histopathology and histochemistry of dermatologic lesions in the mouth. *Oral Surgery, Oral Medicine, Oral Pathology.* 1961;14(9):1069-84.
- Andreasen JO. Oral lichen planus. 1. A clinical evaluation of 115 cases. *Oral Surg Oral Med Oral Pathol.* 1968;25(1):31-42.
- Williams BG. Oral drug reaction to methylidopa. Report of a case. *Oral Surg Oral Med Oral Pathol.* 1983;56(4):375-7.
- Gange RW, Jones EW. Bullous lichen planus caused by labetalol. *Br Med J.* 1978;1(6116):816-7.
- Ferguson MM, Wiesenfeld D, MacDonald DG. Oral mucosal lichenoid eruption due to fenclofenac. *J Oral Med.* 1984;39(1):39-40.
- Lind PO, Hurlen B, Stromme Koppang H. Electrogalvanically-induced contact allergy of the oral mucosa. Report of a case. *Int J Oral Surg.* 1984;13(4):339-45.
- Gupta P, Mallishery S, Bajaj N, Banga K, Mehra A, Desai R. Low Prevalence of Amalgam-Associated Lichenoid Lesions in the Oral Cavity: A Prospective Study. *Cureus.* 2022;14(2):e22696.
- Agha-Hosseini F, Gholamrezayi E, Moosavi MS. Patch test of dental materials in Oral Lichen Planus with considering the role of

- saliva. *Sci Rep.* 2021;11(1):8264.
15. Lehner J, Agbo-Godeau S, Bertolus C. A Retrospective Study of 23 Cases: Are Lichenoid Lesions of the Labial Mucosa Induced? *Cureus.* 2022;14(5):e25012.
16. Tsushima F, Sakurai J, Shimizu R, Kayamori K, Harada H. Oral lichenoid contact lesions related to dental metal allergy may resolve after allergen removal. *J Dent Sci.* 2022;17(3):1300-6.
17. Koch P, Bahmer FA. Oral lesions and symptoms related to metals used in dental restorations: a clinical, allergological, and histologic study. *J Am Acad Dermatol.* 1999;41(3 Pt 1):422-30.
18. Andrei M, Tovu S, Parlatescu I, Gheorghe C, Pirvu C. Correlation of corrosion resistance of dental alloy restorations with oral lichen planus pathology. *Materials and Corrosion.* 2016;67(8):882-7.
19. Seno K, Ohno J, Ota N, Hirofuji T, Taniguchi K. Lupus-like oral mucosal lesions in mercury-induced autoimmune response in Brown Norway rats. *BMC Immunol.* 2013;14:47.
20. Jha V, Workman CJ, McGaha TL, Li L, Vas J, Vignali DA, et al. Lymphocyte Activation Gene-3 (LAG-3) negatively regulates environmentally-induced autoimmunity. *PLoS One.* 2014;9(8):e104484.