

Salted Fish and Their Impact on Oral Health: A Risk for Lichen Planus

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Background: Oral Lichen Planus (OLP) is a chronic inflammatory autoimmune disease of oral mucosa that decreases a patient's quality of life because of the inconvenience and pain. Etiology OLP is still unknown but related to T-cell mediated disease. OLP is also related to allergic reaction or hypersensitivity. Nitrosamine commonly found in processed foods, like salted fish, contains nitrite and nitrate compound known to cause chronic irritation and inflammation in oral mucosa.

Purpose: This case report analyzes correlation between OLP and salted fish consumption.

Case Presentation: A 41-year-old woman presented with complaints of a painful oral ulcer and redness persisting for six months, with symptoms worsening during eating and speaking. The pain typically intensified following the consumption of salted fish. Intraoral examination revealed multiple reticular white plaques, along with diffuse erosive and ulcerative lesions on the oral mucosa. The patient was diagnosed with reticular, erosive, and ulcerative types of OLP.

Case Management: Treatment for the ulcers are antiseptic mouthwash and topical corticosteroid, and also multivitamin to increase patient's health.

Conclusion: Nitrosamine and Formalin that contained in salted fish may be the risk factors of OLP. Eliminating risk factors is necessary to increased successful rate in treatment and prevent OLP's recurrency.

Keywords: food preservatives, formalin, hypersensitivities, oral lichen planus, salted fish

Introduction

Oral lichen planus (OLP) is an autoimmune disease whose etiology is still unknown. The skin and mucous membranes are the most frequently affected parts. OLP appears as white and red lesions, bilaterally, depending on the severity of the disease. OLP is regarded as an oral potentially malignant disorder (OPMD), with a controversial malignant transformation rate, owing mainly to its restrictive diagnostic criteria. Recent studies have documented a malignant transformation rate ranging from 0.44% to 2.58%, with an increased malignant transformation risk in cases of erosive and/or atrophic lesions, tongue lesions, greater intake of alcohol/tobacco, accompanying hepatitis C virus infection, and elderly females in an age range of 60–70 years.¹ In the literature, the prevalence of OLP is around 0.5% and 2% in different populations. Oral lesions occur in 50–60% of lichen planus patients. OLP occurs more in women than men with a ratio of 3:2.² The etiology of OLP is still unknown, but the immune system plays an important role in this disease. This autoimmune disease targets epithelial cells, especially those in the basal layer. This is supported by the histopathological picture, which shows subepithelial infiltration dominated by T lymphocytes and macrophages and basal cell apoptosis. The diagnosis of OLP can be made from the clinical and histological pictures. Biopsy examination is highly recommended to confirm the clinical diagnosis and eliminate the possibility of malignancy. Histologically, OLP shows ortho- or parakeratosis, epithelial dysplasia, apoptotic keratinocytes in the basal layer, band-like lymphocytic infiltration on the connective tissue surface, and vasculolization in the basal cell layer. In addition, direct immunofluorescence examination can be performed to eliminate pemphigus vulgaris, paraneoplastic pemphigus, and pemphigus bullosa. A patch test is carried out to determine the possibility of a type IV allergic reaction.³

Salted fish is a processed product combining salting and drying methods. The use of salt functions as a preservative. Salted fish is made by brining (soaking the fish in a salt solution for a certain time), dry-salting (mixing the fish with salt and drying it), pickle curing (the fish is mixed with salt then stored for a certain time), increasing the normal amount of salt in fresh fish.⁴

Nitrites, nitrates, and other salts are added in food preservation to improve color, taste, and shelf life and to reduce microbial interference. N-Nitrosamine compounds are formed when nitrosation agents in food products interact with nitrites and nitrates that have been added to the food. N-nitrosamine, which is classified as a carcinogen by the IARC and US EPA, can be found easily in a variety of foods.⁵ N-nitrosamine is a reaction of nitrogen oxides and secondary amines but can also be formed during fermentation. Apart from the benefits of nitrites and nitrates in food, increasing nitrosamine content in the body may endanger health. The benefits of nitrites in food are undoubted, but the risk-benefit analysis is the focus of problems in their use as preservatives. Nitrosamines can cause irritation and injury due to the method of use, dose and frequency of exposure. Nitrosamines are very easily formed in acidic conditions or high temperatures from frying or baking.⁶

Formalin is a non-food preservative that is now widely used to preserve food. Formalin is very dangerous for health, not only providing short-term effects such as nausea. Vomiting, diarrhoea, and so on, but it also causes long-term effects, such as injury to the kidneys, lungs, and cancer. Several studies show that salted fish sold in several regions in Indonesia contains formaldehyde. The use of formalin makes salted fish look better and last longer.⁷

Despite the common consumption of salted fish, the potential link between formaldehyde and nitrosamine exposure and the onset or worsening of OLP has been minimally explored. This case report investigates the possible association between salted fish, containing these harmful substances, and the development of OLP, emphasizing the need to consider environmental risk factors in disease management.

Case Report

A 41-year-old female patient came to the Department of Oral Medicine with complaints of mouth ulcers and redness in the mouth that felt sore and painful when eating and talking for six months ago. Patients also complain of a decreased sense of taste. The pain of canker sores once subsided, but then came back. The patient used hyaluronic acid mouthwash and consumed multivitamins, but the pain did not improve. There are no systemic history of hypertension, diabetes, ulcers, and allergies. The patient's last visit to the dentist was 4 months ago to have upper front teeth removed. The patient brushes teeth and tongue twice a day, while bathing in the morning and afternoon. She consumes less fruit and vegetables. She preferred processed drinks than mineral water. Smoking habits and alcohol consumption were denied.

The patient's general condition is good with *compos mentis* awareness. Vital signs examination was normal. Extra-oral examination showed a symmetrical face, dry and exfoliative lips with desquamation at the corners of the upper and lower lips, painless, lymph nodes were not palpable and painless, temporo-mandibular joint examination showed no abnormalities. Intra-oral finding (Figure 1a and b) on the left buccal mucosa (Figure 1c), right buccal mucosa, labial mucosa (1a and 1b) and left lateral of tongue (Figure 1e) showed diffuse reticular white plaque with irregular edges, measuring ± 15 mm, ± 7 mm, ± 3 mm, and ± 10 mm, could not be scrapped, painless. There was an irregular erythematous macule with diffuse borders, measuring ± 5 mm, painless, near the corner of the mouth. Palate showed a painful diffuse erythema spot measuring ± 10 mm near the left maxillary tuberosity. Left lateral (Figure 1d) and ventral tongue (Figure 1f) showed a single oval-shaped ulcer measuring ± 2 mm and ± 3 mm, with irregular edges, yellowish white, surrounded by an erythematous area. There is a diffuse erythema spot measuring ± 10 mm on the ventral tongue extending laterally to the left tongue and the tip of the right tongue, painful.

The patient was diagnosed with exfoliative cheilitis, reticular type oral lichen planus, erosive and ulcerative on the lower labial mucosa, right and left buccal mucosa, dorsum of the tongue, right and left lateral tongue, ventral tongue, palate. In this case, OLP diagnosed with only by clinical examination because the patient cannot provide a patch test and biopsy due to economic issue. Lupus erythematosus and pemphigus vulgaris have the similarity with OLP. These disease were ruled out because there are no sloughing lesion in this case. The prognostic of this case is bonam or good. Non-pharmacological therapy consists of instructions for cleaning the teeth and tongue using a soft-bristled toothbrush twice a day in the morning after breakfast and at night before bed. Education is given to patients to avoid spicy foods, salted

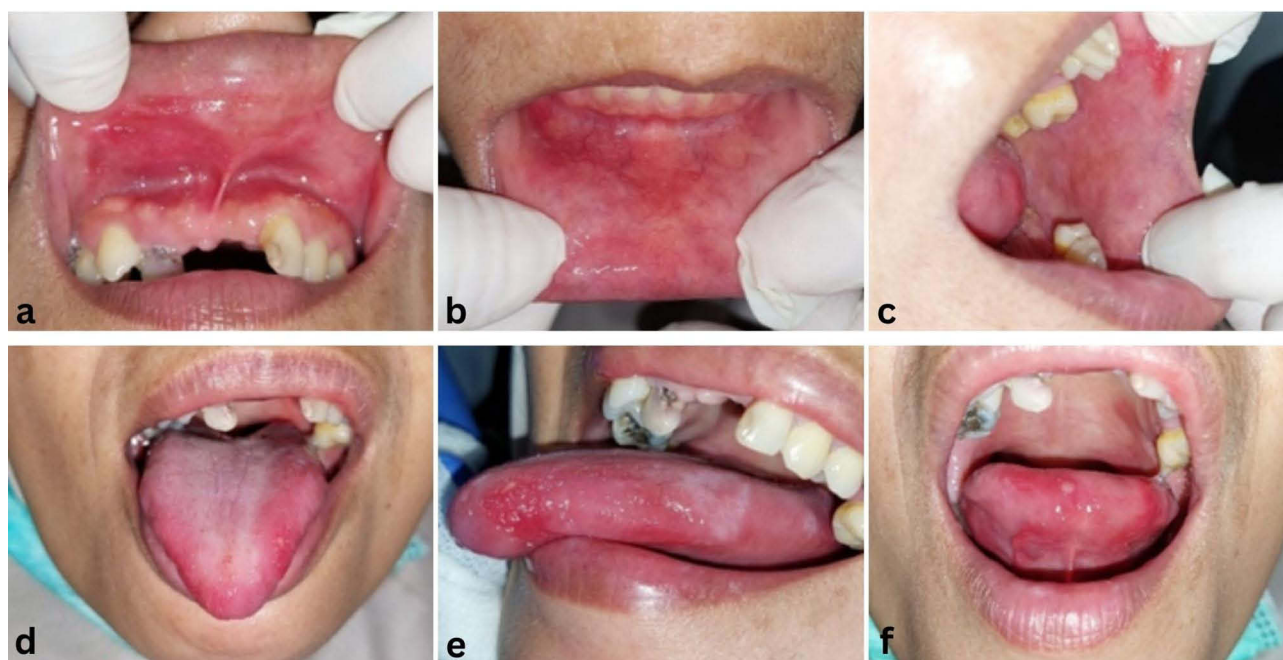


Figure 1 Clinical Appearance in 1st visit. (a-c,e) diffuse reticular white plaque. (d,f) single oval-shaped ulcer.

fish, and consume at least 2 liters of drinking water, regularly consume fruit and vegetables, and get enough sleep. Pharmacological therapy consists of gargling with methylprednisolone powder dissolved in 10 mL of distilled water, 2 pulveres (8mg) in the morning and 1 pulveres (4mg) in the afternoon, gargling for 1 minute then discarding, leaving for 5 minutes then rinsing with water. After that, apply a thin layer of triamcinolone acetonide 0.1% in orabase on white plaque in the lower lip 3 times a day. Spread a thin layer of vaseline on the upper and lower lips at least 3 times a day.

At the second visit, the patient's pain had decreased, but the canker sore had appeared on the upper right inner lip for 2 days ago and painful. Previous prescribed medicines have been used according to the instructions. On clinical examination, it was seen that up and lower labial mucosa, left buccal mucosa, dorsum of the tongue, left lateral tongue, ventral tongue, improved from the first visit (Figure 2a-f). Patients were asked to control after 7 days, and to undergo hematology examination, IgE, IgM and anti-HSV1 tests.

The third visit was carried out 7 days after the second visit. The patient felt that the pain had decreased, but redness appeared on lower labial mucosa, anterior, lateral, and ventral of the tongue, painful since 2 days ago (Figure 3a-d). The patient's habit is consuming fried salted fish. According to the patient's statement, complaints of redness on the tongue appeared the day after the patient ate salted fish. The patient really likes to eat salted fish as a side dish. Non-pharmacological therapy is continued and the patient is asked to stop consuming salted fish until condition in the oral cavity are resolved properly. Pharmacological therapy, the dose of gargling with methyl prednisolone is reduced to 1 pulveres (4 mg) in the morning and 1 pulveres (4 mg) at night, dissolved in 10 mL of aquades. Gargle for 1 minute then spit, leave it for 5 minutes then rinse with water. Triamcinolone acetonide 0.1% and vaseline album are still used as the previous dose. The patient was asked to control 7 days later, and to undergo hematology, IgE, IgG and Anti-HSV1 examinations.

Fourth visit, 14 days after the last visit. The patient said the pain complaint had improved. Consumption of salted fish has been stopped. Clinical examination showed improvement of the lesion (Figure 4a-d). Non-pharmacological therapy was continued. The pharmacological therapy of gargling methylprednisolone is reduced to once a day (4 mg) dissolved in 10 mL of aquades, in the morning.

Discussion

Lichen planus (LP) is a chronic inflammatory disease of the skin and mucous membranes, occurring between the ages of 30 and 60 years, more often in women. LP lesions on the skin usually resolve on their own, but oral mucosal lesions have

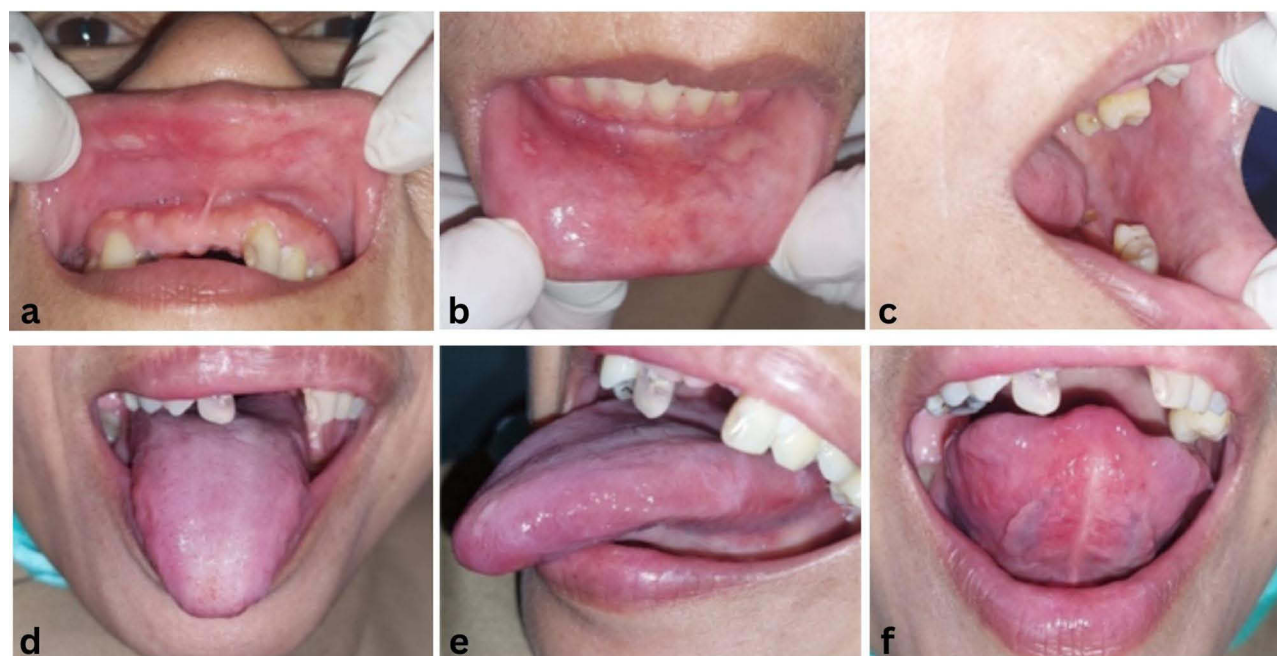


Figure 2 Clinical appearance in 2nd visit. (a–f) healing process after first treatment.

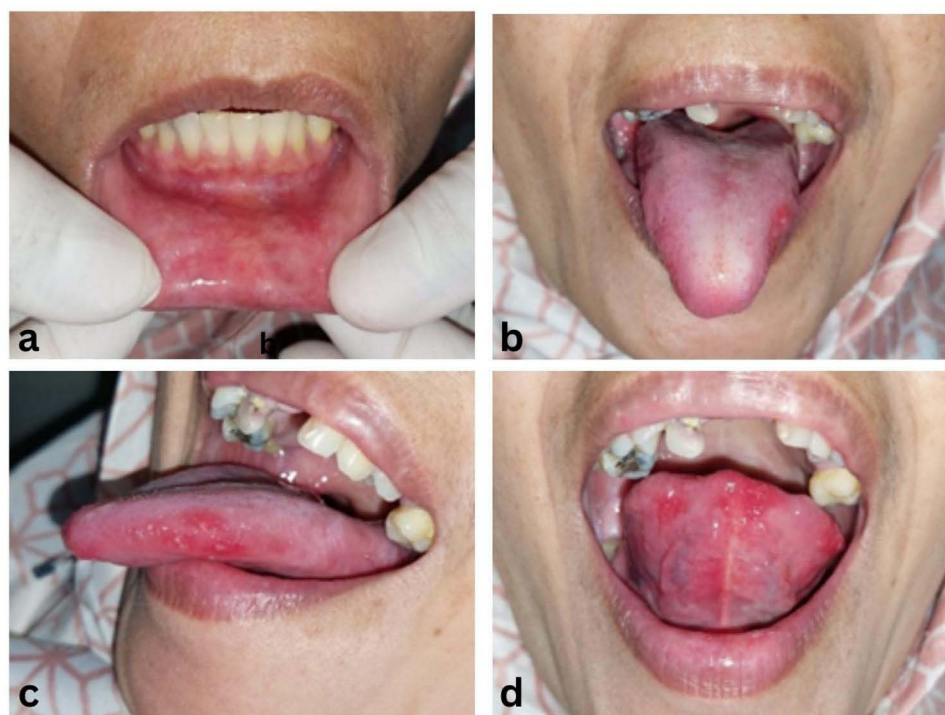


Figure 3 Clinical appearance in 3rd visit. (a–d) the erythema lesion resurface after consumed salted fish routinely.

phases of remission and exacerbation. The clinical picture of OLP varies from the asymptomatic reticular to the painful and uncomfortable erosive type. OLP can occur solidly or with involvement of other skin or mucosal lesions.⁸ OLP can be white (reticular, papular, and plaque-like) or red (erosive, (ulcerative), atopic (erythema), and bullae). The most common lesions are reticular, erosive, papular, and plaque-like. The reticular type usually has no symptoms, while the



Figure 4 Clinical appearance in 4th visit. (a–d) healing process after pharmacology treatment and stopped consuming salted fish.

atrophic, erosive and bullous types give a burning and painful sensation, as complained by patients. OLP is usually bilateral, symmetrical, and most commonly occurs in the buccal mucosa (80–90%), gingiva, and tongue. Lesions rarely occur unilaterally, on the palate, lips or floor of the mouth.² Biphasic process primarily mediated by T lymphocytes cytotoxic mechanism in response to exogenous or self-altered antigens presented by antigen-presenting cells, such as dendritic cells (DCs) and keratinocytes. Tissue-resident memory T cells act as a local reservoir of chronic inflammation, since they can be activated repeatedly, causing LP flares. Regulatory T cells, that physiologically participate in immunosurveillance and suppression of effector T lymphocytes, are defective in LP, hence preventing successful disease control. The action of matrix metalloproteinases (MMPs), mast cells and chemokines contribute to nonspecific immune mechanisms within the disease. The diagnosis of OLP can be decided based on clinical and histological features, however in this patient a histological examination was not carried out due to cost issue, so the diagnosis was decided based on clinical features. OLP treatment depends on the severity of the lesion. For mild lesions such as those in this patient, topical corticosteroids are usually sufficient. For more severe OLP lesions, systemic corticosteroids and perilesion injections are added, but the use must be monitored because they may have serious side effects if used for a long period of time.⁹

The etiology of OLP is still unknown, but the immune system has an important role in the development of this disease so that OLP is one of the autoimmune diseases. In the process, CD8⁺ T lymphocytes are responsible for the process of keratinocyte apoptosis in the basal cell layer, which then causes OLP clinical lesions. OLP can also occur due to chronic irritation, both mechanical and chemical.

Preservatives are food additives to prevent or inhibit fermentation, acidification, or other decomposition of food caused by microorganisms. Preservatives permitted for food include benzoic acid, Na-benzoic acid, K-benzoic acid, propionic acid, sorbic acid and their salts. Preservatives that should not be added to food products include formaldehyde, borax, boric acid and salicylic acid.¹⁰ In other study, consumption of salted fish, salted vegetables and preserved/cured meat were all risk factors for Nasopharyngeal Carcinoma (NPC).¹¹

N-nitrosamines are compounds that are formed during the food manufacturing process. This compound occurs due to the natural reaction of nitrosation agents such as nitrite or nitrogen oxide and secondary amines, which are formed in

various types of food. Nitrates or nitrites are usually added when preserving food, such as meat and fish. Some nitrosamines are genotoxic (damage DNA) and carcinogenic (cause cancer). Several food products contain nitrosamines, such as traditional Chinese salted fish, dry-cured mackerel, grilled meat, and others. Nitrosamine concentrations tend to increase with time, as well as high temperatures such as when cooking.¹²

Formaldehyde or what is commonly called formalin is a dangerous chemical for humans so its use is prohibited as a food raw material, but there are still many food producers who use formaldehyde as an additional ingredient in preserving food.¹³ Antoni found that 2 out of 10 samples (20%) of salted fish from Panam and Arengka markets contained formaldehyde.⁷ Habibah found that 9 out of 41 samples (21.9%) of salted fish from Semarang traditional markets contained formaldehyde.¹⁴ Fatimah et al found that 12 of 26 samples (46.5%) of salted fish from the Giwangan and Beringharjo markets in Yogyakarta contained formaldehyde.¹⁰ The increasing presentation of salted fish containing formalin increases the author's suspicion that OLP in these patients is caused by formalin and is less likely caused by nitrosamine. However, there are limited supporting examinations to determine the patient's hypersensitivity to formalin, namely the patch test, which cannot be carried out due to limited costs, so the diagnosis of OLP in patients is based on the history and clinical picture.

Conclusion

Salted fish is a food whose production process involves preservation using salt and drying. This can cause the formation of N-nitrosamines. The content of nitrosamine compounds will increase when the salted fish to be consumed is cooked first. Formalin, which is currently widely added as a preservative for salted fish, can also trigger the emergence of OLP. Exposure to nitrosamine or formalin when consuming salted fish regularly can cause irritation of the oral mucosa. OLP can appear due to chronic irritation that occurs continuously and causes inflammation. Treatment for OLP, apart from using topical corticosteroids, also involves eliminating risk factors, in this case, namely stopping consumption of salted fish.

Consent Statements

The patient has approved and written informed consent for the publication of this case report, including the images. The institution has also approved the publication of this article.

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Disclosure

The authors report no conflict of interest in this work.

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