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**MANAGEMENT OF ULCERATIVE ORAL LICHEN PLANUS PREDISPOSED BY  
 PSYCHOLOGICAL STRESS**

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**ABSTRACT**

**Background:** Oral lichen planus (OLP) is a chronic inflammatory autoimmune oral mucosa disease. The ulcerative type of OLP presents as erythematous ulceration with mucosal erosions surrounding whitish striae. The aetiology of OLP is unknown, but can be predisposed by psychological factors. **Purpose:** Reporting ulcerative oral lichen planus predisposed by psychological stress. **Case:** A 36 years old woman complained very painful ulcer in the right buccal mucosa and a grey-purple lower lip lesion for a year. It had been treated with topical corticosteroids, antibiotics, tretinoin, and vitamins but did not heal. Extraoral examination on the lower vermilion showed bluish-purple macules, diffuse and irregular borders, rough and painful. Intraoral examination in the right buccal mucosa showed an irregular yellowish-white ulcer with an erythematous area and white striae. **Case Management:** Screening for psychological stress by DASS 42 showed moderate stress and severe anxiety. Autofluorescence examination showed no malignant transformation sign. A complete blood count test showed low neutrophil and lymphocyte count. ANA test was normal. Systemic Methyl Prednisolone 8 mg was prescribed 2 tabs twice a day and tapered off after the lesion resolved within 1 week. Supportive treatments include Benzylamine HCl and multivitamins. **Discussion:** Stress, anxiety, and depression were possible factors of OLP mediated by the Hypothalamic-pituitary-adrenal (HPA) axis system and the Sympathetic-adrenal-medullary (SAM) system. Specific mechanisms are mediated by Antigen-specific CD8+ (CTLs) that are activated with the help of CD4+ T-cells. Non-specific mechanism mediated by MMP-9 activation. They led to the apoptosis of keratinocytes. Systemic corticosteroids are an important treatment for oral lichen planus that do not responded to topical steroids. **Conclusion:** Oral Lichen Planus is a chronic inflammatory disease that affects the oral mucosa and can be predisposed by psychological stress. Corticosteroid is very effective to treat oral lichen planus, especially the erosive-ulcerative type.

**Keywords:** Oral Lichen Planus, Psychological Stress, Ulcerative

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**INTRODUCTION**

Oral lichen planus (OLP) is a chronic inflammatory autoimmune oral mucosa disease. The worldwide prevalence of 1.01% with the risk of malignant transformation being 1.2%. Conversely, cutaneous lesions occur in 10–15% of persons with OLP. The proportion of women is higher than that of men, with a ratio of 3:2. The condition usually occurs in people older than 40 years, with the mean age of onset being 53 years.<sup>1</sup> The aetiology is unclear, but some studies showed it mediated by T-cell.<sup>2</sup>

Stress, anxiety, and depression are factors for the emergence of the possibility of OLP, even though the relationship is still controversial. Some studies show a positive relationship between psychological stress and OLP, although other studies showed no significant relationship.<sup>3</sup> The previous study using the Depression Anxiety Stress

Scale (DASS -42), found a higher frequency of psychiatric disorders like depression, anxiety, and stress in OLP patients in comparison to the control group.<sup>4</sup>

The ulcerative type of OLP presents as erythematous ulceration with mucosal erosions surrounding whitish striae. The base of the ulcer is deep and covered with a pseudomembrane. If it involves the tongue, it will cause dysgeusia. The diagnosis of OLP is based on clinical features and confirmed by histopathological findings if a change in the direction of malignancy is suspected.<sup>5</sup>

OLP is one of the premalignant conditions that need an early diagnosis to reduce morbidity and mortality, especially in a chronic lesion that did not respond to medication. Diagnostic aids have been developed for the early detection of oral cancer using autofluorescence.<sup>6,7</sup>

Thus, this paper aims to report a case of oral lichen planus due to psychological factors based on DASS-42 screening and oral malignant transformation screening using autofluorescence.

### CASE

A 36-year-old female patient complained of canker sores on the right inner cheek and pain in the lower lip since one year ago. Initially exposed to a toothbrush, it became small canker sores, enlarged, and never healed. The patient never had a similar complaint before. Initially, she complained of a bluish-purple colour on the right lower lip, which gradually spread to all parts of the lower lip. The patient had treated these lesions with triamcinolone acetonide 0,1% for a year, Clindamycin phosphate 1.2%, tretinoin 0.025%, and vitamin C 1000 for 5 days, but did not heal.

The patient had no history of systemic disease. The history of drug consumption includes birth control pills, herbal tamarind turmeric, and some herbal medicine. Her father suffers from gout, and her mother has a history of hypertension. Extraoral examination on the lower vermilion showed bluish-purple macules, diffuse borders, irregular edges with multiple dark brown crusts with clear boundaries, ragged edges, and rough and painful surfaces. Intraoral examination showed the right buccal mucosa a single yellowish-white ulcer with clear borders, and irregular edges surrounded by a diffuse reddish area with multiple white striae (Figure 1). There are no lesions on the skin or other mucosa. The clinical diagnosis was OLP ulcerative with a differential diagnosis of discoid-LE and Pemphigus vulgaris.

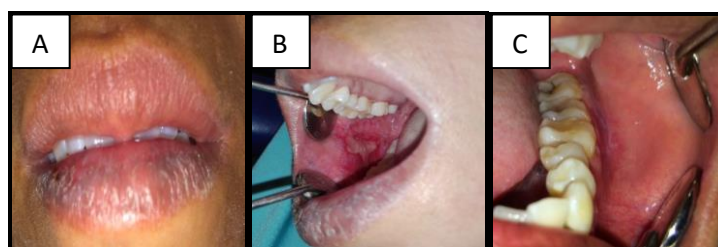


Figure 1. Extraoral & intraoral examination in 1<sup>st</sup> visit A. Brownish black lesions and white striae on vermilion lips. B. An ulcerated lesion with white striae and a reddish area on the right buccal mucosa. C. Lesion of white striae and a red area on the left buccal mucosa (Source: Personal Documentation)

### CASE MANAGEMENT

The first treatment has been prescribed a mouthwash containing *Aloe vera* and multivitamins orally. The patient was instructed to stop all drugs and herbs, use prescribed drugs regularly, maintain oral hygiene, and eat nutritious foods, then referred to examine complete blood count, kidney and liver function test, blood glucose test, and ANA test to exclude the diagnosis of lupus erythematosus. Autofluorescence examination to determine the malignant transformation. The DASS 42 test screening tools for psychosomatic involvement.

On the second visit, the patient came with the complaint that the pain had decreased somewhat and the lips were not too stiff compared to the first visit. The drug has been routinely used.

The patient admitted that there is white plaque and felt rough in the left buccal mucosa. Extraoral and intraoral examinations as showed in (Figure 2).

The results of screening using the Depression Anxiety Stress Scale 42 (DASS 42) obtained a stress scale of 19 (moderate), anxiety 22 (very severe), and depression 6 (normal). A complete blood count showed a low neutrophil count (55% with a reference value of 55-65%) and a high lymphocyte count (41% with a reference value of 25-35%), while other tests showed normal. SGOT, SGPT, BUN, Creatinin level was normal. ANA Test showed Negative (7,53 units). Autofluorescence examination showed no malignant transformation (Figure 3). The final diagnosis is Ulcerative Oral Lichen Planus.

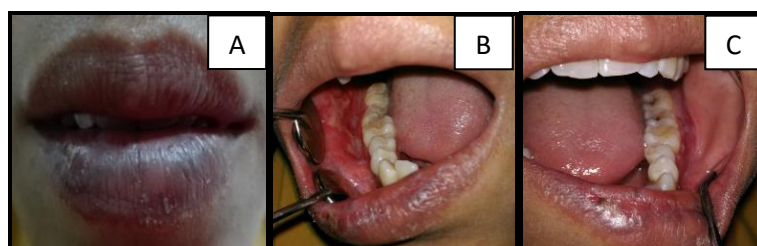


Figure 2. Extraoral & intraoral examination in 2<sup>nd</sup> visit A. Purplish-black macule and squama in inferior labia. B. Single ulcer in an erythematous area and radiating white striae in the right buccal mucosa. C. Erosive area with white striae in the left buccal mucosa (Source: Personal Documentation)

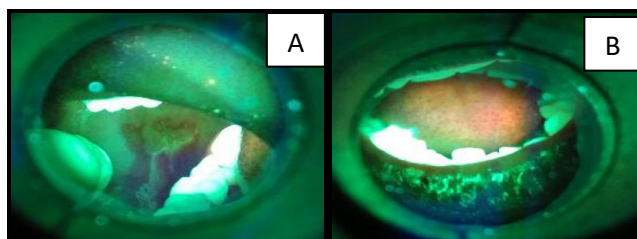


Figure 3. Examination using autofluorescence showed A. Dark orange-red color in the buccal mucosa, B. brownish-orange on the lower lip (Source: Personal Documentation)

Treatment was given methylprednisolone orally 8 mg 4 times a day (32 mg/day), Benzylamine HCl 0.15% mouthwash used 3 times a day, and multivitamins containing vitamins A, B1, B2, B6, B12, C, D, E, nicotinamide, Calcium pantothenate, potassium iodide, iron, magnesium, manganese, copper, and Zn.

Third visit, pain in the right cheek has decreased, but the right cheek still feels rough, and

the gums still feel a little sore, while the lower lip no longer feels stiff. Patients regularly take medication. Extraoral and intraoral examinations as showed in (Figure 4). As the lesion slightly resolved, methylprednisolone was tapered off 8 mg 3 times a day (24 mg/day), Benzylamine HCl 0.15% mouthwash was used 3 times a day, and multivitamins once a day. The patient suggested visiting a psychiatrist, but she refused.

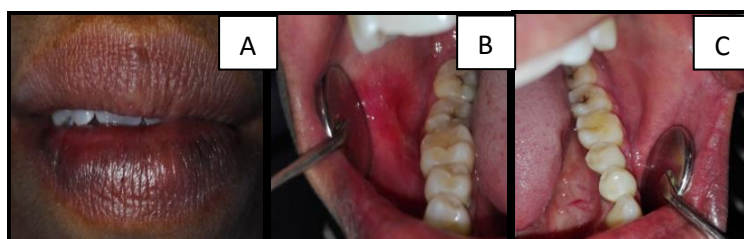


Figure 4. Extraoral & intraoral examination in 3<sup>rd</sup> visit A. Black grayish macule inferior labia. B. Erythematous area and radiating white striae in the right buccal mucosa. C. White striae in left buccal mucosa. (Source: Personal Documentation)

On the fourth visit, the patient still feels a burning sensation sometimes and still feels rough when touched with the tongue. The lower lip is no longer stiff, but has mild pain when given gentle pressure. The medicine has been taken regularly but

mouthwash is only used when it hurts. Extraoral and intraoral examinations as showed in (Figure 5). The methylprednisolone treatment was tapered off to 4 mg twice daily (8 mg/day) and Benzylamine HCl mouthwash 0.15% 3 times a day.

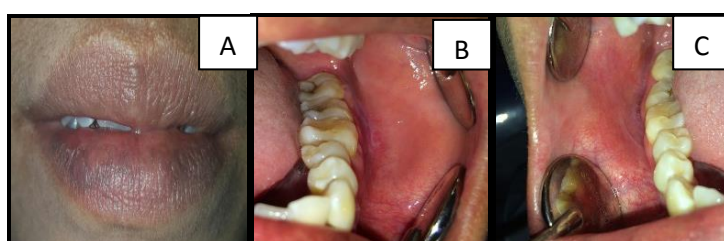


Figure 5. Extraoral & intraoral examination in 4<sup>th</sup> visit A. Diffuse macule inferior labia. B. Little area and white striae in the right buccal mucosa. C. White striae in left buccal mucosa (Source: Personal Documentation)

On the 5<sup>th</sup> visit Complaints of pain when eating decreased. The patient admitted that he was no longer stressed about his family's condition because his child had started to be independent. The methylprednisolone treatment was tapered off to 4 once per day. Mouthwash and Multivitamins were discontinued and patients were instructed to eat nutritious foods and avoid spicy foods.

On the 6<sup>th</sup> visit, the patient had no complaints, and the lesions improved. Extraoral and intraoral examinations as showed in (Figure 6). IEC treatment is always to maintain oral hygiene, consult if complaints, eat nutritious food, especially vegetables and fruit, and self-management psychological stress. Lesions resolved within 8<sup>th</sup> weeks.

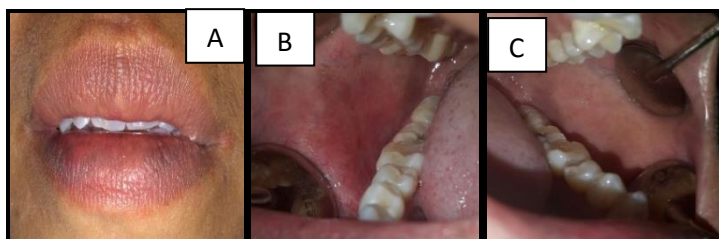


Figure 6. Extraoral & intraoral examination in last visit A. More diffuse macula inferior labia. B. Diffuse red area in the right buccal mucosa. C. No lesion in left buccal mucosa (Source: Personal Documentation)

## DISCUSSION

Oral lichen planus (OLP), a precancerous lesion involving the mucous membranes and skin, primarily affects women in the 6th or 7th decade. OLP is usually bilateral and involves the buccal mucosa, tongue, gingiva, lips, and palate. OLP can affect several areas of the oral cavity.<sup>8</sup>

Stress, anxiety, and depression have often been identified as factors associated with OLP although some are still controversial. Psychological stress occurs when a person feels the demands of the surrounding environment exceed his abilities. Anxiety is an emotion recognized and regarded as a feeling of anxiety or panic and is accompanied by physical changes such as an increase in blood pressure. Depression is a common psychological disorder that is often characterized by sadness, loss of interest in the environment, guilt or low self-esteem, sleep disturbances, loss of appetite, tiredness, and lack of concentration.<sup>3</sup>

Based on the results of the DASS 42 examination, it is known that the patient experienced moderate stress and severe anxiety. She admitted that for the last few years, the patient had felt anxious and stressed because of his family's financial condition, but she refused to be referred to a psychiatrist due to distance, time, and cost constraints so she tries to manage stress and anxiety by herself.

### The Process Of OLP In Patients Experiencing Stress

Stress influences the pathogenesis through direct effects on biological processes or behavioural patterns that lead to increased disease risk. Psychological stress also activates 2 endocrine response system. First is the Hypothalamic-Pituitary-Adrenal (HPA) axis, where stress and trauma increase stress hormones and cortisol, which control many physiological processes such as the anti-inflammatory response. Second, the Sympathetic-Adrenal-Medullary (SAM) system where catecholamines, neuropeptides, and neurotrophic released in response to SAM activation, can alter the immune response and reduce lymphocyte function in the skin and mucosa.<sup>9,10</sup>

The pathogenesis of OLP occurs through specific and non-specific mechanisms. Typical mechanisms include LP antigen expression and association with MHC class I molecules on basal

keratinocytes. Antigen-specific CD8+ cytotoxic T-lymphocytes (CTLs) are activated with the help of CD4+ T-cells and trigger keratinocyte apoptosis through the binding of TNF- $\alpha$  to TNF- $\alpha$  receptor. However, granzyme B and Fas also play a role in this stage. Activated TNF- $\alpha$  is secreted across the CTL surface via Matrix Metalloproteinase (MMP).<sup>10,11</sup>

Meanwhile, non-specific mechanisms through activated T cells perform clonal expansion and release RANTES and other cytokines that increase CCR1 expression of mast cells and stimulate migration and degranulation of mast cells into the lesion. Degranulated mast cells secrete TNF $\alpha$ , which increases the expression of endothelial cell adhesion molecules for lymphocyte adhesion and extravasation. Mast cell-derived TNF- $\alpha$  also increases RANTES and MMP-9 secretion. Activated T cells in the lesion (and keratinocytes) secrete chemokines that attract extravasated lymphocytes to the OLP-affected epithelium. Mast cell degranulation releases chymase that damages the epithelial basement membrane directly or indirectly through MMP-9 activation. Damage to the epithelial basement membrane facilitates more lymphocytes to enter the epithelium and prevents the survival of the keratinocyte signal. This condition leads to further apoptosis of keratinocytes.<sup>12</sup>

### OLP clinical features

There are 6 kinds of clinical features of OLP: papular, reticular, plaque-like, atrophic, erosive, and bullous. The clinical picture can be of one type or several forms in a single lesion with a characteristic appearance of radial white-lined papules around the lesion (Wickham's striae). Although the clinical picture may vary, the lesions are primarily bilateral and mainly involve the buccal mucosa. In addition, it can affect the tongue, vestibule, and gingiva.<sup>13</sup> In the case above, the right buccal mucosa was ulcerative, erosive, and reticular papules (Wickham's striae) that extended from the buccal mucosa to the vestibule and gingiva. The lesion was erosive and intermittent reticular extending from the vestibule to the gingiva on the right buccal mucosa. The entire attached gingiva was reddish, but there were no complaints. The presence of a characteristic appearance of Wickham's striae indicates the diagnosis of an OLP.



Lesions on the lips mainly affect the lower lip, although occasionally the upper and lower lips and most rarely only the upper lip. Erosive lichen planus of the lip causes localized sharp pain, whereas scarring lichen planus causes lip atrophy and in chronic cases, causes microstomia. In addition, the appearance of lichen planus on the lips always persists in the vermillion. It does not spread to the skin in the form of an erythematous area surrounded by diffuse, diffuse, lace-like white keratotic lines with greyish-white papules along the vermillion. This condition can be necessary for differentiating between cheilitis and lupus erythematosus. Ring-like lesions are rarely found on the lips. In black patients, the center of the lesion is usually hyperpigmented.<sup>14</sup>

#### **OLP Supporting Examination**

Autofluorescence is a tool that can observe the abnormalities in the oral mucosa by activating tissue autofluorescence. Autofluorescence occurs due to endogenous fluorophores in cells that produce fluorescent emissions when exposed to light with specific wavelengths. In the oral mucosa, the most abundant fluorophores are nicotinamide adenine dinucleotide and flavin adenine dinucleotide in the epithelium and collagen of the stroma. Abnormal mucosa can alter absorption and light-emitting properties due to changes in tissue composition and levels of fluorophores. In addition, conditions such as mucosal pigmentation, ulceration, irritation, and gingivitis also display a dark colour under autofluorescence.<sup>15</sup> The above patient was screened using autofluorescence because the lesions that did not heal and persisted for the 1 year were suspected of leading to malignancy; then, the examination results showed a purple-orange red colour while the lower lip appeared brownish orange. This picture shows inflammation under the lesion due to increased vascularity and hyperpigmentation of the lower lip. The base of the ulcer looks yellowish-orange due to the accumulation of pseudomembranes and bacteria and inflammation around the ulcer.

A complete blood count showed a low neutrophil count and a high lymphocyte count, while other tests showed typical results. Low neutrophils can occur in conditions of the use of drugs/chemicals that suppress the bone marrow. In addition, the presence of infection, liver disorders, collagen-vascular diseases such as lupus erythematosus and folic acid and vitamin B12 deficiency, while high lymphocytes occur in conditions of illness, metabolic disorders, chronic inflammation, and autoimmune disease. Examination of ANA Test to rule out the suspected diagnosis of Lupus Erythematus and the results are typical so that the lesion is not Lupus Erythematosus. Assessment of kidney function, liver function, and blood sugar showed specific results,

and the systemic condition was good, so corticosteroids could be given. If the suspected malignancy does not show improvement after 2 weeks, a biopsy should be performed to establish a definite diagnosis.<sup>16</sup> However, in this case, the lesion responded to corticosteroid therapy in less than 2 weeks, so a biopsy was not performed.

#### **OLP Treatment**

Topical steroids are recommended as the primary symptomatic therapy in OLP patients because the long-term treatment has minimal side effects. Topical therapy can be combined with systemic steroid therapy.<sup>17</sup> Methylprednisolone tablets 2 times a day, then the dose was gradually reduced after an improved response to the lesion. These treatments were to minimize steroid side effects. Steroids work by suppressing T cell function and reducing IgG synthesis. When inflammation is suppressed, tissue damage is reduced, and antigen secretion is minimized. Steroids do not affect hyperkeratotic lesions, but strongly affect erosive and atrophic lesions both locally and systemically and quickly relieve symptoms.<sup>18</sup>

In addition, the patient was given a multivitamin supplement containing vitamin A, B1, B2, B6, B12, C, D, E, nicotinamide, Capantothenate, potassium iodide, iron, magnesium, manganese, copper, and zinc. Vitamins A, C, and E can improve the function of the epithelial/skin barrier. Apart from vitamin C, all vitamins are also crucial for antibody production. In addition, vitamins B6, B9, B12, A, and D also increases the production of cytokines and T lymphocytes.<sup>19</sup>

Aloe vera mouthwash was given at the initial visit containing Aqua, maltodextrin, propylene glycol, polyvinylpyrrolidone (PVP), aloe vera extract, potassium sorbate, sodium benzoate, hydroxyethylcellulose, PEG 40, hydrogenated castor oil, disodium edetate, benzalkonium chloride, saccharin sodium, sodium hyaluronate, glycyrrhizic acid. Materials that can accelerate the healing of canker sores include Polyvinylpyrrolidone (PVP) which can function as an antibacterial and reduce infection, and gibberellins, which are known to interact with growth factor receptors on fibroblast cells, thus increasing the activity and proliferation of wound contractions in the wound healing process.<sup>20</sup>

Benzylamine HCl mouthwash is a non-steroidal drug with anti-inflammatory, analgesic, anaesthetic, and antimicrobial effects. Benzylamine HCl is widely used and very effective for treating oral mucositis due to radiation therapy or chemotherapy. Benzylamine HCl inhibits the production of TNF- $\alpha$  and IL-1. The mechanism of action is still unclear, but it may work by suppressing the production of prostaglandins and thromboxane and reducing the production of pro-inflammatory cytokines.<sup>21,22</sup> OLP

is a chronic inflammatory disease caused by an autoimmune process that attacks the oral mucosa and can be triggered by psychological stress. Corticosteroids are effective in treating oral lesions of OLP, especially the erosive-ulcerative type. In addition, to avoid triggering factors, patients need to understand the management of stress experienced or referred to psychiatry.

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