

# Multidisciplinary Management of Recurrent Aphthous Stomatitis Triggered by Severe Depression

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## ABSTRACT

**Background:** Recurrent Aphthous Stomatitis (RAS) is an inflammation of the oral mucosa in the form of a single or more ulcer that occurs repeatedly. One of the predisposing factors that contribute to the onset of RAS is depression. Depression is a mood that is not happy or sadness that is experienced as part of the pattern of life. **Objective:** Discuss multidisciplinary management in cases of 65-year-old women with large multiple ulcers with depression-triggering factors. **Case:** Women aged 65 years complained of recurrent canker sores. The frequency of RAS increased by 10 years due to economic and household problems. It has been treated with topical non-steroidal anti-inflammatory drugs but does not heal. Does not have a history of systemic diseases. **Case Management:** Do investigations are complete peripheral blood examination, Depression Anxiety Stress Scale (DASS), Refer patients to the psychiatric specialist. Multidisciplinary treatment is performed by a psychiatric specialist. Treatment of oral mucosa with topical anti-inflammatory steroid drugs. **Conclusions:** in accordance with the treatment that has been given, this case has recovered after day 14. So it can be concluded that proper multidisciplinary management and elimination of triggering factors are the main roles to prevent recurrence and reduce the frequency of recurrent aphthous stomatitis.

**Keywords:** Recurrent Aphthous Stomatitis (RAS), Ulcer, Depression, Depression Anxiety Stress Scale (DASS)

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## INTRODUCTION

Recurrent aphthous stomatitis (RAS) is an inflammation of the oral mucosa that occurs repeatedly. RAS is one of the most common oral diseases. RAS is a reserve in the oral mucosa with a worldwide prevalence of 5-25%. RAS mostly occurs at the age of 10-40 years and many occur in women. The main characteristics of RAS are the presence of painful and reoccurring ulcers on the oral mucosa.<sup>1,2,3</sup>

RAS is divided into three types, minor, mayor and herpetiform. Minor RAS has characteristics such as small ulcers with a diameter of less than 4mm. This type of RAS has a healing process that lasts about 7-14 days without scarring. While Major RAS is a large ulcer with a diameter of more than 10 mm, and the healing process requires period of 2-12 weeks accompanied by scarring. The Herpetiform RAS is multiple ulcers numbering 10-100 ulcers with a diameter of about 1-2 mm.<sup>4,5</sup> The clinical appearance of RAS consists of round or oval, single or multiple, ulcers, yellowish- white understood as halo erythematous, painful and recurred.<sup>6</sup>

Until now the etiology of the RAS is unclear. The emergence of RAS is related to several triggering factors such as hematinic deficiency (iron, folate, and vitamin B12), hormonal, age, sex, hypersensitivity to food and medicine, family, trauma, nutrition, hormones, and stress.<sup>4</sup> Several studies have revealed that stress has a close relationship with RAS, where there is a relationship with cortisol and reactive oxygen species (ROS). The RAS also opposes changes in the immune system, namely modifications that affect many immune systems such as the distribution, proliferation and activity of lymphocytes and natural supporting cells, phagocytosis, and the production of cytokines and antibodies.<sup>4,7</sup> The purpose of this paper is to describe a case report about the management of recurrent Aphthous Stomatitis that is triggered by stress.

## CASE

A 65-year-old woman came to the Dental Clinic of Universitas Airlangga Surabaya with chief complaints of sore mouth on the buccal mucosa referred from a poly prosthodontist. From the history, it is known that sore mouth appeared 3 days ago after being impress using alginate ingredients. Patients have a history of recurrent sore mouth since young, increasing in the last 10 years or so. The patient treats sore mouth by gargling warm salt water. The patient loses all of the maxillary and mandibular teeth beginning with cavities until the extraction of all her teeth. Have used dentures since 7 years ago but are loose and uncomfortable. The patient is a housewife who also works in a canteen. Patients feel they do not have allergies. The family has no history of allergies. The patient has no history of systemic disease.

The general condition of the patient looks thin and weak. Examination of vital signs of tension, pulse, respiration, and temperature normal. Extra-oral examination of the right submandibular gland feels soft and painless. The left submandibular gland is not palpable. There were no lesions or complaints in the eyes, skin, and genitals. Intra-oral examination of the buccal mucosa dextra appears ulcer, single, oval-shaped, size 3x9mm, central yellowish-white, clear borders, irregular edges, normal surrounding area, and pain. Based on the history and clinical examination, the working diagnosis of this case is Recurrent Aphthous Stomatitis triggered by trauma.



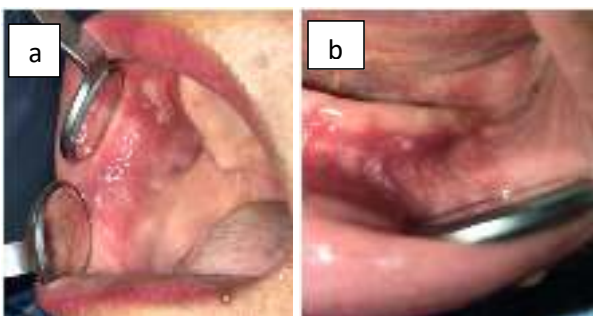
Figure 1. Single ulcer in the right buccal mucosa



Patients were given symptomatic therapy containing steroids with topical cream prescription applied 4x per day (Triamcinolone Acetonide 0.1% in ora base). Information and Education Communication to patients to improve oral hygiene, instructions to use medication appropriately and regularly, patient instructions carefully with the location of the lesion, patient instructions to improve high-calorie and high-protein soft food diets, increase vegetable and fruit intake Get enough rest and rehydration. Patients were scheduled for control 7 days later.

In the first control, a sore mouth on the right inner cheek has slightly disappeared and not too painful. Two days ago a new sore mouth appeared on the upper inner cheek, appearing suddenly. The patient's claimed stress in economic matters and the husband who had an affair. Patients use oral medication regularly. Patient's diet is irregular, only 1 time a day, and rarely drinks water. The patient's rest is still lacking, the patient claimed to have difficulty sleeping.

Extra-oral examinations normal. Intra-oral examination showed the presence of ulcers, multiple, in the buccal mucosa dextra oval, with sizes 3x9 mm and 2x7mm, the central yellowish-white, clear boundary, irregular edges, the area around normal, pain. in the edentulous ridge anterior of the mandible there is an ulcer, round shape, measuring 5mm, yellowish-white, irregular edges, the area around normal, pain.



**Figure 2.** a. Multiple ulcers in the buccal mucosa dextra. b. Single ulcer in the lower jaw gingiva

For diagnosis, the patient is instructed to conduct a supporting examination, namely a complete peripheral blood examination, blood sugar examination during, examination of HBA1c, SGOT, SGPT, and Ig E Total. The patient was examined for Depression Anxiety Stress Scale (DASS). The results of blood tests showed high blood sedimentation rates, eosin, lymphocytes, total IgE, and HBA1c. While the segment, MCH, and MCHC are low. Other blood tests appear normal. Based on the results of the DASS scoring examination the patient is in a state of severe depression, very severe anxiety and, severe stress. Based on the history, clinical examination, and supporting examination to eat a working diagnosis of this case is Recurrent Aphthous Stomatitis that is triggered by stress.

Patients were given symptomatic therapy containing steroids with topical cream prescription applied 4x per day (Triamcinolone Acetonide 0.1% in ora base). Patients are also prescribed multivitamins once a day. Information and Education Communication to increase oral hygiene, instructions to use medication appropriately and regularly, patient instructions to avoid contact with lesion locations, patient instructions to improve high-calorie and high-protein soft food diets, increase vegetable and fruit intake, eat slowly, adequate rest, and rehydration. Calms the patient regarding the problem being faced. Patients were referred for prick tests and referred to a medical specialist (Psychiatrist). Patients were scheduled for control 7 days later.

The second control (14 days), sore mouth the edentulous ridge and buccal mucosa has healed. Oral ointments are used routinely 3 times a day. But because it was cured the patient stopped using the drug himself. The patient had gone to a psychiatrist, the patient was diagnosed with a Severe Depression Episode and was prescribed Fluoxetine, Zipren and Clobazam. Patients consume drugs according to the rules and regularly. Extra-oral examinations appear normal, body temperature normal, palpation of the left and right submandibular glands appear

normal. The normal intra-oral examination has no lesions.



**Figure 3.** a Mucosa Right buccal & b. Lower anterior gingival normal

Based on the history, clinical examination, supporting examination and inter-clinical integration, the final diagnosis of this case is Aphthous Recurrent Stomatitis triggered by severe depression. Information and Education Communication to patients to increase oral Hygiene by cleaning the tongue, instructing patients to improve high-calorie and high-protein soft food diets, increasing vegetable and fruit intake, eating slowly, getting enough rest, and rehydration. Patients are encouraged to remain in control of a psychiatrist. If there are complaints in the oral cavity the patient is recommended to control again.

## DISCUSSION

Stress can be considered as a psychophysiological process that is a product of evaluating certain situations to assess potential difficulties and the ability to overcome potentially harmful situations. Events that have the potential to be a threat are called stressors. The situation is obtained from experiences in daily life, including daily busyness. Stressors often occur from interaction with family, school environment or workplace. Stress can be in the form of mental/ psychological stress and physical stress, in this patient psychological stress occurs, and is supported by physical stress.<sup>6</sup> Based on duration, stress can occur acutely (minutes to hours and days), subacute (duration less than one month), or chronic (months to years). based on intensity, acute stress that has a high intensity

can have longer lasting effects.<sup>7,8,9</sup> Based on the duration and intensity of stress experienced by the patient is recurring chronic stress.

Depression Anxiety Stress scale (DASS) is a question designed to measure the level of negative emotions of depression, anxiety, and stress. The stress scale in the depression anxiety stress scale consists of 14 questions and is very sensitive to the level of non-specific chronic causes. The stress scale is used to measure the level of relaxation, the emergence of nervous disorders, the level of anger, excessive reaction, and the level of patience. The results of respondents answers based on stress felt by individuals that cause efforts to react to the stress they experience. Stress is a manifestation of the relationship between environmental events or conditions with an individual's cognitive assessment of the level, type of challenge, difficulty, loss, and threat. The reaction is an activity to adjust to certain stimulant situations, which if it cannot be done properly will cause physical and psychological disorders. In these patients, the DASS results were depression 21 (severe), anxiety 27 (very severe), and stress 23 (severe).<sup>10,11</sup>

In stressful conditions, the adrenal cortex will secrete cortisol which will cause a decrease in IFN-produksi production and increase IL-10 and IL-4 production which will trigger a change in the balance of pro-inflammatory and anti-inflammatory cytokines more towards the proinflammatory response. However, recent research states that it is this dysregulation of cytokine balance that plays an important role in linking the effects of stress on the immune system. There are several immune responses that occur in RAS, namely a decrease in the number of CD4 lymphocytes and changes in the ratio of CD4: CD8, decrease in regulation of CDreg CD4 Tregs, increase in B lymphocyte counts, increase in T cell counts, decrease HSP expression, increase in complement system, increase in NK cell counts, reactivation and hyperreactivity of neutrophils, decreased expression of anti-inflammatory cytokines produced by Th2 and TGF $\beta$ , increased





expression of pro-inflammatory cytokines produced by Th1 and IL-2, IL-12, IFN-gamma and TNF $\alpha$ .<sup>12,13</sup>

In the humoral response, levels of salivary IgA in patients with RAS show an increase in the acute period and decrease in the period of regression and healing. In addition to IgA, there is an increase in IgG and IgM levels. IgG and complement work together to help each other as opsonin in antigen destruction. IgG has effective opsonin properties because phagocyte, monocyte and macrophage cells have receptors for the Fc fraction of IgG so that they can strengthen the relationship between phagocytes and target cells. These changes can lead to pathological conditions in the oral mucosal epithelial cells, so that epithelial cells are more sensitive to stimulation.<sup>12</sup>

The impact of stress on the immune system through the relationship between the brain and the immune system involves two main pathways, namely: Autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal (HPA) axis. Perception of stress causes activation of the HPA system which starts with secretion of corticotrophin releasing hormone (CRH). CRH induces secretion of adrenocorticotrophic hormone (ACTH) by the anterior pituitary lobe. ACTH activates cortisol secretion by the adrenal cortex and catecholamines (adrenaline and noradrenaline) by the adrenal medulla. Catecholamines and cortisol suppress the production of IL-12 by antigen-presenting cells which are the main induction stimulus for cytokine TH1. Cortisol can also have a direct effect on TH2 cells thereby increasing IL-4, IL-10 and IL-13 production. The end result is an imbalance between TH1 and TH2. This condition is dominated by TH2 cells which will support the inflammatory response to release.<sup>7,9,13</sup>

Based on the history, clinical examination and supporting examination, the final diagnosis in this case is Stomatitis Aphthous Recurrent triggered by stress. The non-pharmacologic management in this case is referring the patient to a psychiatric specialist to

be given therapy which is expected to reduce the level of depression as a triggering factor. In addition, topical oral drug therapy containing corticosteroids was given, namely triamcinolone acetonide. Acetonide is a moderate to high potency corticosteroid, a fluorinated prednisolone derivative and is considered a glucocorticoid with intermediate-act glucocorticoids having anti-inflammatory effects. Glucocorticoids decrease the production of cytokines, chemokines, and increase the production of macrophage migration inhibitory factors. As an anti-inflammatory, glucocorticosteroids will pass through the membrane by diffusion. In cell membranes, glucocorticosteroids will be captured by their receptors (GR) and assisted by heat shock protein-90 (hsp90). As anti-inflammatory glucocorticosteroids can be through 2 pathways. The first pathway, glucocorticosteroids with receptors will directly activate anti-inflammatory proteins. the second path, will enter the nucleus. In the nucleus, it inhibits the transcription of NF- $\kappa$ B in producing inflammatory proteins. this is the reason we give Triamcinolone acetonide to suppress the inflammatory process and accelerate the healing process of the lesion.<sup>3,14,15</sup>

## CONCLUSION

RAS is an inflammation of the oral cavity that often occurs. RAS can be triggered by several factors, one of which is psychological stress which can alter the immune system and body tissues and reducing mucosal resistance. The main therapy is to eliminate the causative factors / predisposing factors and followed by the therapy needed to relieve pain and speed healing.

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