Journal of Indonesian Oral Medicine Society
Vol 2 no 3, October 2024, p. 13-19
Submitted on 23 September 2024, Accepted on 20 October 2024

CASE REPORT

Interplay of Stress and Gastroesophageal Reflux Disease: A Case Study of Recurrent Aphthous Stomatitis

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ABSTRACT

Background Recurrent Aphthous Stomatitis (RAS) is a common and painful oral mucosal condition characterized by recurrent ulcerations. While its exact aetiology remains multifactorial and not fully understood, predisposing factors such as psychological stress and systemic conditions like Gastroesophageal Reflux Disease (GERD) have been implicated in its recurrence and severity. This case report explores the clinical course and multidisciplinary management of RAS in a patient with underlying GERD and elevated stress levels. **Case report** A 24-year-old female presented with recurrent, painful oral ulcers, primarily occurring before menstruation. The patient also had a medical history of GERD and reported high stress levels due to a demanding lifestyle. Clinical examination revealed minor aphthous ulcers on the buccal mucosa, while laboratory findings were within normal references. Management involved a comprehensive therapeutic plan that included topical anti-inflammatory and antiseptic agents, multivitamins, improved oral hygiene practices, dietary modification, and stress reduction through regular exercise. Significant clinical improvement was observed following treatment. **Conclusion:** This case highlights the importance of a holistic, patient-centred approach in managing RAS, especially when systemic conditions such as GERD and behavioural factors like stress are involved. Long-term monitoring and interprofessional collaboration are crucial for achieving and maintaining sustained remission and an improved quality of life.

Key words: recurrent aphthous stomatitis, GERD, stress, oral ulcers

INTRODUCTION

The oral mucosa serves as a critical protective barrier, safeguarding the oral cavity against physical trauma, infectious agents, and carcinogens. Despite its protective function, it remains susceptible to a range of pathological conditions and lesions. While some lesions may appear benign in certain individuals, they can lead to significant complications in others.[1] Among the most frequently encountered oral lesions is the aphthous ulcer, a form of ulceration that is typically painful and may disrupt essential oral functions such as mastication and phonation. These disruptions can negatively impact an individual's social interactions and compromise daily nutritional intake. The pain associated with these lesions often results from the loss of epithelial integrity in the soft tissues of the oral cavity, which can further impair the function of the stomatognathic system.[1,2]

One of the most common ulcerative disorders of the oral mucosa is Recurrent Aphthous Stomatitis (RAS), a self-limiting condition marked by the recurrence appearance of painful ulcers with variable presentation and duration among individuals. Although most cases resolve spontaneously within a few days, the recurrent nature of the condition can be distressing. The global prevalence of RAS ranges from 5% to 66%, with an average of approximately 20%.[2,3] It tends to occur more frequently in individuals from middle to high-socioeconomic backgrounds. Despite being non-life-threatening and non-contagious, RAS can significantly impair quality of life, especially in cases of frequent recurrence or severe symptoms.

Clinically, RAS is characterized by recurrent, painful ulcerations of the oral mucosa and can affect individuals across all age groups. It manifests in three distinct clinical forms: minor, major, and herpetiform. Commonly affected sites include the labial mucosa, buccal mucosa, and dorsal surface of the tongue. RAS is widely recognized as a multifactorial condition involving dysregulated, T cell–mediated immune responses. A variety of contributing factors may trigger or exacerbate the condition, including genetic susceptibility, viral and bacterial infections, food allergies, deficiencies in vitamins

DOI: xx.xxxx/jioms.xxxx
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and trace elements, systemic diseases, hormonal fluctuations, mechanical trauma, psychological stress, and overall nutritional deficiencies.[2–5]

An effective strategy to reduce the recurrence of Recurrent Aphthous Stomatitis (RAS) involves identifying and avoiding predisposing factors. Currently, RAS treatment is primarily palliative, focusing on alleviating pain, minimizing lesion size, and promoting mucosal healing. Management strategies encompass local therapy, systemic pharmacological interventions, and supportive non-pharmacological measures. Local therapy typically involves applying topical agents to reduce inflammation and prevent secondary infection. In more severe or refractory cases, systemic treatment may be warranted. Pharmacologic agents include nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids such as prednisolone, immunomodulators like pentoxifylline, and diaminopiphenyl sulfone antibiotics like dapsone. Additionally, supportive therapy with multivitamin supplementation, such as multivitamin with high dose of B vitamin, which possesses antioxidant properties, may enhance mucosal repair and bolster the immune response.[5]

CASE REPORT

A 23-year-old female patient presented with a chief complaint of painful oral ulcerations localized on the right and left buccal mucosa, which had developed over the previous two days. The pain was particularly exacerbated during mastication, impairing normal eating function. During anamnesis, the patient reported a history of recurrent aphthous ulcers occurring approximately once per month, typically in the premenstrual phase. She also described suboptimal dietary habits, including infrequent consumption of fruits and vegetables, frequent consumption of spicy foods, and limited hydration with an average water intake up to 2 litres per day.

The patient's medical history was notable for Gastroesophageal Reflux Disease (GERD), and a known allergy to Sulfamethoxazole. Additionally, she reported a high daily workload and psychosocial stress, which may contribute to immunological dysregulation and recurrent mucosal ulceration.

Extraoral examination revealed no significant abnormalities. Intraoral examination identified two ulcerative lesions: one on the right buccal mucosa measuring 3×2 mm and another on the left buccal mucosa measuring 5×2 mm. Both lesions were shallow, surrounded by erythematous halos, and consistent with minor aphthous ulcers. Additionally, a non-removable white coating was observed on the posterior third of the dorsal surface of the tongue, indicative of coated tongue.

Figure 1. Clinical images obtained during the first visit
revealed 2 ulcers on right and left buccal mucosa (yellow circle)

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Based on the patient's clinical presentation, including both subjective complaints and objective findings, a working diagnosis of Recurrent Aphthous Stomatitis (RAS) was established. Differential diagnoses considered included traumatic ulcer, herpes zoster, and herpes labialis. Management was initiated with a multifaceted therapeutic approach: local treatment with hyaluronic acid mouthwash to facilitate mucosal healing, antiseptic therapy using 0.2% chlorhexidine gluconate to prevent secondary bacterial infection, and supportive care with a multivitamin containing B vitamins to promote tissue regeneration and enhance immune function.

The patient received comprehensive counselling on lifestyle and behavioural modifications in conjunction with pharmacologic therapy. Emphasis was placed on the importance of a balanced diet rich in fruits and vegetables, adequate hydration (at least 2 litres of water daily), and consistent oral hygiene practices—brushing twice daily, tongue cleaning, and the use of dental floss—to minimise mucosal irritation and support overall oral health.

Stress management was also identified as a critical component of care. The patient was encouraged to engage in regular physical activity and incorporate stress-reducing practices such as mindfulness or relaxation techniques. Given the potential role of psychological stress and Gastroesophageal Reflux Disease (GERD) in the pathogenesis and recurrence of RAS, an integrated management strategy addressing both systemic and local factors was considered essential for long-term disease control and prevention of recurrence.

As part of the initial diagnostic workup, a complete blood count (CBC) was performed to assess potential systemic factors contributing to the patient's condition. Laboratory results revealed that haemoglobin, hematocrit, leukocyte, and platelet levels were all within normal physiological ranges, thereby supporting the exclusion of hematologic abnormalities and systemic infection as contributing factors.

Examination	Result	Reference Value	Unit
Hemoglobin	12,9	12,0 - 15,0	g/dL
Hematokrit	40	36 - 44	%
Leukosit	8,5	4,0 - 11,0	$10^3/\mu L$
Trombosit	304	150 - 450	$10^3/\mu L$

At the second follow-up visit, on 28 August 2024, a week after the initial presentation, the patient returned for reassessment. She reported partial improvement, with complete resolution of the ulcer on the left buccal mucosa, while the lesion on the right buccal mucosa persisted. Clinical examination revealed a single ulcer on the right buccal mucosa, measuring approximately 3×3 mm, with an irregular contour and well-demarcated borders. No signs of secondary infection were observed.

Her oral hygiene was assessed to be within moderate standards. There was no evidence of dental plaque, calculus, or extrinsic staining. A yellowish-white coating was noted on the posterior dorsum of the tongue, which could be mechanically removed, consistent with a diagnosis of coated tongue. The gingiva displayed physiological pigmentation in certain areas, and no additional mucosal abnormalities were identified.

The patient reported consistent adherence to the prescribed therapeutic regimen, including oral rinsing with 0.2% chlorhexidine gluconate twice daily, administered upon waking and before bedtime, and continued use of previously recommended topical agents and multivitamin supplementation. The resolution of the lesion on the left buccal mucosa was interpreted as a favourable therapeutic response. At the same time, the persistence of the right-sided ulcer indicated the need for continued management.

Continuing the current pharmacologic therapy was advised as the initial treatment plan. The patient was re-emphasised on the importance of maintaining a nutrient-rich diet, and minimising the consumption of irritant foods such as spicy items. Lifestyle modifications were reinforced as integral to the long-term management of Recurrent Aphthous Stomatitis (RAS) and associated systemic

conditions. A follow-up appointment was scheduled for one month later to evaluate complete lesion resolution and monitor for recurrence.

Figure 2. Clinical images obtained during the second visit with new lesion appeared on the right buccal mucosa (yellow circle)

At the third follow-up visit, the patient reported no further complaints related to oral ulceration. Intraoral examinations revealed no active lesions or new ulceration. The right and left buccal mucosa appeared completely normal, with no evidence of ulcers, erythema, or other abnormalities. The patient also reported significant improvements in her dietary habits, including a reduction in the consumption of spicy foods, an increase in the intake of fruits and vegetables, and consistent daily hydration as recommended.

The patient's oral hygiene practices had notably improved, with regular use of 0.2% chlorhexidine gluconate mouthwash twice daily and consistent tooth brushing. While a yellowish-white coating remained on the dorsum of the tongue, consistent with a diagnosis of coated tongue, no signs of secondary infection or irritation were noted.

Additionally, the patient demonstrated progress in managing stress, which was identified as a key predisposing factor for recurrent aphthous ulcers in this case. Regular physical exercise made a positive contribution to her overall stress management as part of her lifestyle modifications.

Overall, the clinical evaluation indicated significant improvement in the patient's condition since the initial visit. The complete resolution of oral ulcers and the positive effect of the lifestyle changes highlight the efficacy of the comprehensive management approach. Long-term monitoring and continued adherence to the recommended health practices are essential to ensure sustained improvement and prevent the recurrence of major recurrent aphthous stomatitis.

Figure 3. Clinical images obtained during the third visit show that all of the lesions have already healed

DISCUSSION

Gastroesophageal reflux disease (GERD) is a prevalent gastrointestinal disorder characterised by the retrograde movement of gastric contents through the lower oesophageal sphincter (LES) into the oesophagus and, in some cases, the oropharynx. Clinical manifestations commonly arise due to exposure of the distal oesophageal mucosa to acidic gastric contents during episodes of reflux. The pathogenesis of GERD is multifactorial. Pathological reflux is believed to result from a breakdown in the equilibrium between the injurious properties of gastric secretions—such as hydrochloric acid, bile salts, pepsin, and duodenal contents—and the oesophagus's natural defence mechanisms, including acid clearance and mucosal resistance. The primary physiological defect underlying GERD appears to be LES dysfunction, which facilitates the reflux of increased volumes of acidic gastric content into the oesophagus. This elevated acid burden exceeds the oesophagal mucosa's protective threshold, resulting in tissue injury and symptomatic disease.[5-8]

GERD may also have systemic implications beyond the oesophagus. There is growing evidence to suggest that GERD may contribute to the development or exacerbation of recurrent aphthous stomatitis (RAS).[8] RAS is a common condition characterised by painful ulcerations of the oral mucosa and is associated with significant impairment in quality of life.[3] In this context, several pathophysiological mechanisms have been proposed to explain the relationship between GERD and RAS.

Firstly, the regurgitation of gastric acid into the oral cavity may directly irritate the mucosal surfaces, creating a favourable environment for ulcer formation. Secondly, GERD is well reported to be related to stress as a psychological trigger. Emotional stress is a well-recognised predisposing factor for RAS, as it can dysregulate immune responses, enhance systemic inflammation, and delay mucosal healing. In patients with concurrent GERD and RAS, chronic stress may exacerbate both conditions simultaneously. Elevated cortisol levels—often observed in stress states—are known to influence immune cell activity, particularly by promoting leukocyte proliferation and inflammatory responses, which may further increase the likelihood of aphthous ulcer recurrence.[4]

According to a study by Hernawati, the interplay between stress and the onset of RAS involves complex neuroendocrine and immunological mechanisms. Stress activates the central nervous system, prompting the hypothalamus to secrete corticotropin-releasing hormone (CRH), which subsequently stimulates the anterior pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH then acts on the adrenal cortex, leading to the secretion of glucocorticoids, predominantly cortisol. This elevation in cortisol modulates immune responses, particularly promoting Th2 lymphocyte activity, which in turn stimulates the release of interleukin-4 (IL-4). IL-4 activates mast cells, basophils, and plasma cells,

resulting in the production of immunoglobulin E (IgE). The subsequent IgE-mediated anaphylactic reaction increases mucosal tissue vulnerability, rendering it more susceptible to minor trauma and, thus, increasing the risk of ulcer formation in predisposed individuals.[2,5,9]

In addition to stress-related immune modulation, hormonal fluctuations may also contribute to the development of RAS. In this patient's case, the occurrence of aphthous lesions preceding menstruation suggests a role for hormonal factors in exacerbating the disease. Research has demonstrated that fluctuations in estrogen and progesterone levels during the premenstrual phase can influence oral mucosal integrity. A study by Ballan et al. found that approximately 30% of women reported RAS onset a few days before menstruation. A decline in estrogen, which plays a key role in promoting the maturation and keratinisation of oral epithelial cells, coupled with a reduction in progesterone—associated with diminished epithelial cell turnover—may compromise the oral mucosa's barrier function, thereby increasing susceptibility to ulceration.[6,10]

Immunological dysregulation is central to the pathogenesis of RAS. Several immune alterations have been implicated, including a reduced CD4+ T-lymphocyte count, an altered CD4:CD8 ratio, impaired activity of regulatory T cells (Treg CD4+CD25+), and increased proliferation of both B and T lymphocytes. Additionally, decreased expression of heat shock proteins (HSP), enhanced complement activation, elevated levels of natural killer (NK) cells, and heightened neutrophil reactivity have all been reported. Cytokine imbalances are also observed, with a reduction in anti-inflammatory mediators such as transforming growth factor-beta (TGF-β) and IL-4 from Th2 cells, along with an upregulation of pro-inflammatory cytokines—including IL-2, IL-12, interferon-gamma (IFN-γ), and tumour necrosis factor-alpha (TNF-α)—produced by Th1 cells.[7]

Laboratory evaluations for this patient revealed haemoglobin, hematocrit, leukocyte, and platelet levels within normal physiological ranges, ruling out haematological abnormalities as contributory factors. The therapeutic approach was structured as follows: Causative Therapy involved the administration of hyaluronic acid as a topical medication to promote mucosal healing and reduce localised inflammation in ulcerated regions. The symptomatic therapy included a prescription for Chlorhexidine gluconate 0.2% mouthwash as an antiseptic to prevent secondary infections and facilitate mucosal repair. Supportive Therapy: A multivitamin supplement was recommended to ensure adequate micronutrient intake, thereby supporting immune function and oral tissue regeneration.

In addition to pharmacological intervention, comprehensive oral hygiene instructions were provided. The patient was advised to brush her teeth twice daily—after meals and before bedtime—and to incorporate tongue cleaning, the use of antiseptic mouthwash, and dental flossing into her daily routine. Nutritional counselling emphasised increased consumption of fruits and vegetables to support soft tissue health and bolster immunity. Physical activity was also encouraged as a means of stress reduction.

At the third follow-up, the patient reported complete resolution of the aphthous lesions, with no recurrence or residual pain. She had adopted dietary modifications, including an increased intake of fruits and vegetables and a reduction in the consumption of spicy foods. Additionally, she maintained adequate hydration by consuming approximately two litres of water daily and had incorporated regular physical exercise into her routine to manage stress.[10]

The patient continued to adhere to her oral hygiene regimen, including twice-daily rinsing with chlorhexidine 0.2%, demonstrating improved oral health awareness and compliance with preventive measures. Her clinical progress reflects a positive response to the multifaceted treatment strategy.

The recurrent nature of aphthous ulcers in this patient was likely the result of several interrelated factors, including dietary deficiencies, psychological stress, systemic conditions such as GERD, and hormonal fluctuations. The successful management of her condition underscores the importance of a holistic, multidisciplinary approach that addresses both local and systemic contributors. Continued follow-up is essential to monitor for recurrence and ensure sustained disease control.

CONCLUSION

Recurrent Aphthous Stomatitis (RAS) is diagnosed based on subjective symptoms and objective clinical findings. The patient's comprehensive medical history may contribute to the development and persistence of RAS. Reducing stress, which can trigger GERD, is a holistic procedure in the management of recurrent aphthous stomatitis. Through an integrated management approach, it is

anticipated that the severity of pain, lesion duration, and frequency of recurrence can be effectively minimised.

CONFLICT OF INTEREST

The authors declare that there were no conflicts of interest related to this case report.

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