

Original Research

Recurrent Aphthous Stomatitis: An Update

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ABSTRACT:

Recurrent aphthous ulcer (RAU) is a clinical condition characterized by painful ulcer with different size affecting the mucosa of the oral cavity. Its etiology and pathogenesis are not clearly known and the diagnosis is based on the clinical picture. These lesions may be classified into minor, major, and herpetiformis. Although RAUs are self limited, this lesion causes pain and discomfort and interferes in eating, speaking, and swallowing which leads to poor quality of life. Early and effective treatment of RAUs ulcer minimizes the discomfort in speaking and painful swallowing. Present review of literature aims to discuss recurrent aphthous ulcer in detail.

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INTRODUCTION

Recurrent aphthous stomatitis, commonly known as aphthous ulcer, is an unfortunately most common disease occurring in oral cavity. It is characterized by the development of painful, recurring solitary, or multiple ulcers in the oral cavity and upper throat. The ulcers are usually multiple, small, round, or ovoid, with circumscribed margins, having yellow or gray floors and are surrounded by erythematous haloes.¹

The term aphthae is derived from the Greek word aphthi, which means “to set on fire” or “to inflame,” and is thought to have been first used by the philosopher hippocrates to describe the pain associated with a common disorder of the mouth during his time (likely, aphthous stomatitis).²

It is one of the most painful oral mucosal inflammatory ulcerative conditions and causes pain on eating, swallowing and speaking.³ The classic presentation of RAS is recurrent, self limiting ulcers that mainly affect non-keratinized oral mucosa. The

ulcers heal spontaneously within 7-14 days. The etiology appears to be multifactorial with numerous causative and precipitating factors.⁴ There is growing evidence that there may be a genetic and immunopathogenic basis for recurrent Aphthous ulceration.⁵

Diagnosis of RAS is almost invariably established on the basis of the patient’s clinical history and presentation of the lesions.⁶ There is no specific treatment for RAS. Management strategies should be determined by disease severity, especially in terms of pain, duration, the patient’s medical history, the frequency of flare-ups and the patient’s ability to tolerate the medication. Most cases can be managed with topical therapy, but systemic therapy is available for patients with major RAS or those who experience large number of minor ulcers and syndrome associated ulcers.⁷

ETIOLOGY OF RECURRENT APHTHOUS STOMATITIS

Several theories describing the etiopathogenesis of RAS have been described in the literature. The pathogenesis of RAS is multifaceted with significant physiological interplay between the immune system, genetics, and environmental factors.

The other possible etiologies are drug use, lack of folic acid, Vitamin B12, iron, and other dietary factors, stress, hormonal changes, metabolic diseases, and infections. RAU is commonly seen oral lesion affecting 5%–66% of the adult patients seen in outpatient department.⁸ There are numerous aggravating factors which are identified for the RAU, but the exact etiology is still unknown. There is difficulty in establishing the exact nature of RAU due to their nonspecific histopathology and absence of any reproducible identifiable cause, i.e., endogenous or exogenous cause.⁹ The extensive investigations on the patients identified a range of local, gastrointestinal, hematological, genetic nutritional, allergic, psychological, and drug reactions as trigger factors in RAU. Certain factors such as interstitial collagenases (MMP-1 and MMP-8) are enzymes that cause degradation of main oral mucosa collagen Type I and Type III, leading to RAU.¹⁰

As the exact etiology of the aphthous ulcer is still not clear, many predisposing factors such as trauma, stress, immunological, and viral infections are taken into consideration. Stress and anxiety are associated with RAU. Stressful condition is thought to increase salivary cortisol and enhance immunoregulatory activity by increasing leukocytes number at the site of inflammation. Psychological stress in RAU might be triggering factor rather than an etiological factor.^{11,12}

PREDISPOSING FACTOR FOR RECURRENT APHTHOUS STOMATITIS

- Genetic Factor:** It is depicted that around 40% of cases have positive family history. Hence it is main pre-disposing factor. These subjects have ulcers owing to genetic may be more severe.¹³
- Trauma:** In dentistry frequent uses of injections may lead to trauma. Trauma due to sharp cusps or hard bristles of brush result into injury finally leading to aphthous ulcers.¹⁴
- Drugs:** Various drugs, especially ACE inhibitors have been found to be analogous with the development of recurrent Aphthous stomatitis. Also some other drugs in the group of non-steroidal anti-inflammatory category such as

diclofenac have been associated with the development of oral ulcers.¹⁵

- Microbes:** In development of RAS, streptococci have been implicated as a major factor. Especially Streptococcus Sanguis have been particularly isolated. Some of ulcers have been detected to have some content of H. pylori but a definite relationship has not been established yet.¹⁶
- Allergy:** Ulcers can be seen in patients allergic to different kind s of foods like chocolates, wheat, tomatos etc. It is also seen in some cases that dentrifices containing sodium lauryl sulfate causing ulcers to some patients.¹⁷
- Stress:** Stress has been implicated as one of the common factors associated with the recurrent aphthous stomatitis. The reason implied is that when a subject is under stress, it leads to the development of the gratuitous habits which involves injury to the oral mucosa. This injury in turn leads to oral aphthous ulcer.⁵

CLASSIFICATION OF RECURRENT APHTHOUS STOMATITIS

- Minor RAS:** It is the most common presentation affecting about 80% of patients with RAS: ulcers are round or oval usually < 5 mm in diameter with a gray–white pseudomembrane and an erythematous halo. Usually occur on the labial and buccal mucosa and floor of mouth, but are uncommon on the gingiva, palate, or dorsum of the tongue. The ulcers heal within 10–14 days without scarring.
- Major RAS:** It is a rare, severe form of RAS, sometimes termed periadenitis mucosa necrotica recurrens. These ulcers are oval and may exceed 1 cm in diameter and have a predilection for the lips, soft palate, and fauces. The ulcers persist for up to 6 weeks and often heal with scarring. Usually has its onset after puberty and is chronic, persisting for up to 20 or more years.
- Herpetiform ulceration:** It is the least common variety and is characterized by multiple recurrent crops of widespread, small, painful ulcers. As many as 100 ulcers may be present at a given time, each measuring 2–3 mm in diameter, although they tend to fuse producing large irregular ulcers. It may have a predisposition for women and have a later age of onset than other types of RAS.¹⁸

	Minor RAS	Major RAS	Herpetiform RAS
Gender predilection	Equal	Equal	Female
Morphology	Round or oval lesions Gray-white pseudomembranes Erythematous halo	Round or oval lesions Gray-white pseudomembranes Erythematous halo	Small, deep ulcers that commonly converge Irregular contour
Distribution	Lips, cheeks, tongue,	Lips, soft palate, pharynx	Lips, cheeks, tongue, floor

	floor of mouth		of mouth, gingiva
Number of ulcers	1–5	1-10	10-100
Size of ulcers	<10mm	>10mm	2–3mm
Prognosis	Lesions resolve in 4–14 days, No scarring	Lesions persist >6 weeks, High risk of scarring	Lesions resolve in <30 days, Scarring uncommon

DIAGNOSIS

There is no definite laboratory test available for establishing the diagnosis of RAU. The histopathological examination does not give a definite diagnosis for this lesion. The diagnosis of RAU is done by considering clinical features and history taking. There are no specific diagnostic tests for RAU. There is need to exclude some possible causes of recurrent oral ulcerations such as Behcet's disease, periodic fever adenitis pharyngitis aphthous ulcer syndrome, and HIV infection. In Behcet's disease, the ulcerative lesions are seen elsewhere, usually on the mucosa such as genitals, eyes, skin, and oral mucosa. The detailed virological tests are usually not warranted unless to rule out atypical herpes infection.¹⁹

MANAGEMENT

The treatment of RAS becomes a frustrating experience for the clinician, as it is extremely difficult to determine the exact cause of the lesion. Hence, the main aim of the clinician is directed towards alleviation of the symptoms and reduction in the severity and duration of the ulcers rather than to address basic issues of susceptibility and prevention.

TOPICAL THERAPY

Topical agents are the first choice of treatment for RAU. They are cheap, effective and safe.

Several pastes and gels can be used to coat the surface of the ulcers and to form a protective barrier against secondary infection and further mechanical irritation. The topical agents are the first option of the treatment of RAS. Patient should apply a small amount of gel or cream after rinsing, and avoid eating or drinking for 30 min. This can be repeated 3 or 4 times daily.²⁰

- **Mouthwashes:** Tetracycline is an antibiotic mouthwash. It reduces the ulcer size, duration, and pain because of the ability of that one to block collagenase activity. Chlorhexidine gluconate is an antibiotic agent may decrease the number of ulcer days. Chlorhexidine can cause brown staining of the teeth and tongue.^{20,21}
- **Local steroids:** Steroids have been commonly implicated as a major treatment option for the canker sores. Usually dexamethasone is prescribed in the dose of 1 mg 3 times a day for 5 days. Cases have shown significant improvement both in the size of the ulcer and the severity of the disease.¹⁵
- **Local anaesthetics and analgesics:** Locally acting symptomatic preparations can relieve

symptoms and decrease the duration of the ulcer attack. Several pastes and gels can be used to coat the surface of the ulcers and form a protective barrier against secondary infection and mechanical irritation. Lidocaine as a 2% containing gel (Gelicaine 2% gel, Xylocaine 2% gel), or as a spray (Xylocaine pump spray), polidocanol as a paste (Solcoseryl adhesive dental paste), and benzocaine in the form of lozenges (Anaesthesin lozenges) can be used.^{22,23}

TOPICAL ANTI-INFLAMMATORY AGENTS

- **Amlexanox:** Topical paste of 5% Amlexanox having anti-allergic and anti-inflammatory activities has been proved to be clinically safe and efficient in several clinical studies for managing RAS.^{24,25}
- **Sucralfate:** A recent study on Italian patients suggested that 20% sucralfate is beneficial in reducing the symptoms of RAS (Campisi et al, 1997).⁵

SYSTEMIC THERAPY

For the severe and constantly recurring ulcerations, may be associated with systemic disease or syndrome, topical management of RAU may not be enough. In these cases, systemic medications are employed.

Severe cases of RAS, immunosuppressive, and anti-inflammatory drugs have shown varying degrees of success. Drugs commonly used include corticosteroids, dapsone, colchicine, thalidomide.²⁶

Severe cases of major RAS may require systemic corticosteroids. Systemic prednisone therapy should be started at 1.0 mg/kg per day as a single dose in patients with severe ulceration and should be tapered after 1 to 2 weeks.²⁷

Dapsone in a dose of 100–150 mg/day can be used for oral and genital aphthae. Haemolysis, methaemoglobinemia and agranulocytosis are serious side-effects that may occur.²¹

Laser therapy (high power and low power) have been used for RAS and reported as case studies and clinical trial studies. In some studies low-level laser therapy had efficacy like or better than topical steroids.²⁸

The symptomatic and supportive treatment is self explanatory and focuses on the current level of patient morbidity. This phase is defined by the prescription of generally proprietary preparation that obvious and major concerns of the patient: (a) antiseptic/anaesthetic preparations; (b) adequate analgesia; (c) maintenance of fluid balance; (d) adequate dietary intake.⁵

Preventive treatment is a consideration for patients who with exacerbations of their condition. It focuses on the prodromal stage, and attempts to intercept ulcer development again by the use of topical immunosuppressants and particularly corticosteroids. Clinical experience shows that many RAU patients will enter a phase of complete clinical remission following the medium term use of a corticosteroid mouth rinse on a daily basis initially and then on a minimal maintenance dose over one to two months.⁵

CONCLUSION

RAS is a multifactorial disease which can occur due to bacterial infections like infection with *Streptococcus sanguis*, immunologic abnormalities, nutritional deficiencies like iron, vitamin B12, folic acid deficiency, and certain precipitating factors like trauma, endocrine conditions, psychic, and allergic factors.

Since the etiology and the pathogenesis of the disease remains unclear, it is extremely imperative that a control of predisposing factors is maintained in order to reduce the chances of suffering from recurrent aphthous stomatitis. Nevertheless, some treatment modalities have emerged in recent years, no definite treatment still exists for the disease. Development of better understanding of the disease and subsequent treatment plan is necessary.

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