Recurrent Aphthous Stomatitis (RAS)

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Abstract

Recurrent aphthous stomatitis are very common painful mucosal conditions affecting the oral cavity. In spite of their high prevalence, etiology remains unclear. The article outlines the clinical presentation, diagnostic criteria, and current trends in the management of recurrent apthous ulcers .

Keywords: RAS , Stress Ulcers, Ulcer Activity Index Immunomodulation , Diagnostic Criteria.

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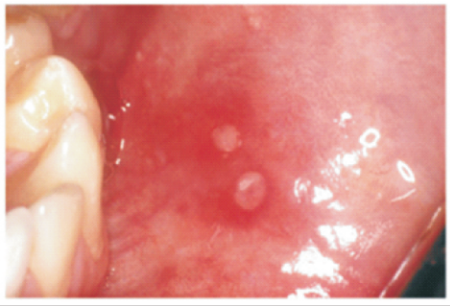
Introduction

The term Aphthous means ulceration. Recurrent apthous stomatitis (RAS) is a common painful oral mucosal condition. The clinical presentation of RAS is small, multiple, round or ovoid ulcers, with circumscribed margins, having yellow or gray floors surrounded by erythematous haloes.[1,2]

Clinical Presentation

The three different clinical variants of RAS as classified by Stanley in 1972.[3] Minor RAS, Major RAS, Herpetiform

A: Minor RAS: It is also known as Miculiz's aphthae or mild aphthous ulcers. It is the most common form, constituting 80% of RAS. Its Size ranges between 8-10 mm in diameter with agreyish, white pseudomembrane and an erythematous halo. Most common Site is labial mucosa, buccal mucosa, and floor of the mouth. These ulcers heal within 10–15 days without scarring.[3]



Typical minor aphthae (buccal mucosa, 22-year-old male

B. Major RAS: Periadenitis mucosa necroticarecurrens or Sutton's disease. 10–15% of patients are affected .these ulcers exceed 1 cm in diameter. Most common Sites : lips, soft palate, and fauces. Last for about 6 weeks and heal with scarring.[4]

Major aphthae (soft palate and fauces, 32-year-old male)

C. Herpetiform: Characterized by recurrent small, multiple ulcers may be up to 100 in number. Size varies between 2–3 mm in diameter. They Combine to form large irregular ulcers Persist for about 10–14 days. Women are commonly affected than males and have a later age of onset as compared to other clinical variants of RAS.[1,3]

Herpetiform ulcers (tongue, 42-years-old female)

Apthous ulcers are further divided as:
Simple and Complex Apthosis

Simple Apthosis: Are few lesions ,heal within 1 -2 weeks, recur infrequently.

Complex Apthosis: Multiple, Severly painful ,of larger size, develop more frequently.

Predisposing factors

- Genetics
- Trauma
- Drugs
- Tobacco
- Hematinic deficiency
- Gluten sensitive enteropathy/celiac disease.
- SLS containing tooth paste.
- Hormonal changes.
- STRESS
- Micro organisms

Genetics

A genetic predisposition for the development of apthous ulcer is strongly suggested as about 40% of patients have a heredity and these individuals experience ulcers earlier and are of more severe nature.[3] several relations /associations with HLA antigens and RAS have been reported. These associations vary with specifc racial and ethnic origins.[4,5]

Trauma

Trauma to the oral mucosa because of local anesthetic injections, dental treatments, sharp tooth. [2]Wray et al. in 1981 evaluated that mechanical injury may aid in identifying and studying patients prone to aphthous stomatitis.[6]

Drugs

Include ACE inhibitor captopril, gold salts and sodium hypochloride. NSAIDS such as, diclofenac, propionic acid may also be the cause of oral ulceration which appear like RAS.[7]

Tobacco

Various studies discovered a negative association between cigarette smoking, smokeless tobacco and RAS. Nicotine is thought to be the protective element as it stimulates the production of adrenal steroids by its action on the hypothalamic adrenal axis and reduces production of (TNF-α) and interleukins 1 and 6 (IL-1 and IL-6).[8,9,10]

Hematinic Deficiency

Iron deficiency, vitamin B12, and folic acid predispose development of RAS.

Gluten sensitive enteropathy/celiac disease, inflammatory bowel disease: Gluten Sensitive ENTEROPATHY, also known as Celiac Sprue , a malabsorbption syndrome has association with RAS. Inflammatory bowel diseases e,g Crohn's disease and ulcerative colitis may present with apthous-like ulceration.[1,2]

Sodium lauryl sulfate (SLS)containing toothpaste: It has been reported that on using sodium lauryl sulfate containing tooth paste there is an increased frequency

in the occurrence of RAS .[2]

Hormonal Changes

Many Conflicting reports exist regarding association of hormonal changes in women and RAU.

However in 1992 McCartan et al [11] confirmed that there is no association between apthous stomatitis and premenstrual period, pregnancy, or menopause.

Stress

It has been emphasized that stress is a causative factor in RAU. Recent study shows lack of interrelation between levels of stress and severity of RAS episodes and revealed that psychological stress may behave as a triggering factor rather than a causative factor in susceptible RAS patients.

Role of Microorganisms in apthous ulceration

RAS and oral streptococci: It has been evaluated that L form of α-hemolytic streptococci, Streptococcus mitis was the causative factor of this disease. Hoover et al. in 1986 [12] discovered that low levels of cross-reactivity of oral Streptococci and oral mucosal antigens and considered the reactivity to be non-specific and clinically insignificant.

RAS and Helicobacter pylori: H. pylori has been implicated as one of the organisms in the etiopathogenesis of RAS.

In 1997 Porter et al.[13] measured the levels of IgG antibodies against H. pylori in patients with RAS and concluded that the frequency of anti-H. pyloriseropositivity was not significantly increased in patients with RAS and other ulcerative and non-ulcerative oral mucosal disorders.

Viruses as etiologic agents in RAS: In 1998 Sun et al. [14]discovered the existence of Epstein-barr virus (EBV) genomes in pre-ulcerative oral apthous tissues in RAU patients by polymerase chain reaction.

Disease	Presentation
Behcet's syndrome	RAU, genital & ocular ulcers
Magic syndrome	Varient of behcets with inflamed cartilage
PFAPA	Periodic fever, apthae, pharyngitis, and cervical adenitis. Seen in young children
Sweet's syndrome/acute febrile neutrophilic dermatosis.	Fever,leukocytosis, skin lesions:dense dermal neutrophilic infiltrate
Cyclic neutropenia	Cyclical neutropenia, Oral ulceration, cutaneous abscess,URTI,LAP.
HIV	Apthouslikenulcerations

Systemic diseases with RAU[1]

Index For Determining Impact of Oralulcer Activity In Patients of RAS: In 2009 Mumucu et al.[15] recommended a combined index to record the clinical manifestations associated with oral ulcers in patients of RAS and Behcet's disease. This index gives us information regarding the prognosis of disease and therapeutic effect of medication. The index contain three variables.

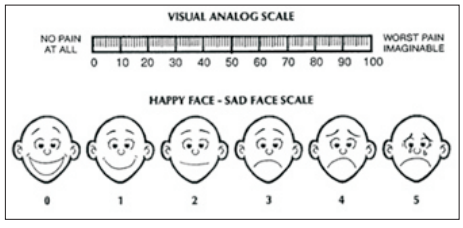
- Oral ulcer activity
- Ulcer related pain
- Functional disability

1.Oral ulcer activity was recorded as number of ulcers in the past 1 month.

0	No ulcers present
1	If the number of ulcer was greater or equal to than one

0	NONE OF THE TIME
1	LITTLE OF THE TIME
2	SOME OF THE TIME
3	MOST OF THE TIME
4	ALL OF THE TIME

2.The pain status was evaluated on a visual analogue scale (VAS).



This is a 100-mm line with extreme values at either end.

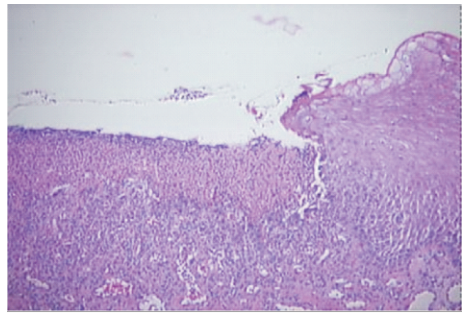
The patients have to mark the intensity of pain on the line

3.Functional status evaluation: This involved the evaluation of effects of oral ulcers on tasting, speaking, and eating/chewing/swallowing. This was assessed by by Likert-type scale.

Use of visual analog scale to evaluate the pain caused by ulcers is highly subjective and is ridden with interpersonal variation. This is a continuous scale with no discrete levels as would be suggested by grades such as none, mild, moderate, or severe. Morestudies in diverse population and ethnic groups need to be executed using this criteria to prove this index.[1]

HISTOPATHOLOGY OF RAS

Histopathology of aphthous ulcer is non-specific/exact. Mucous membrane of shows superficial tissue necrosis with a fibrinopurulent membrane covering the ulcerated area. Necrosis is covered by neutrophils. Epithelium is infiltrated by lymphocytes and few neutrophils. Mononuclear lymphocytes are appreciated in adjacent areas. Minor salivary glands mostly appear in areas of aphthae reveal focal periductal and perialveolar fibrosis and chronic inflammation.[7,16,17]



A central ulcer with a thick fibrin bed containing numerous neutrophils

Shafer's textbook of oral pathlogy 6th edition.

The typical anitschkow cell in a cytologic smear from the margin of an apthous ulcer.it a prodominent cell but not pathognomonic

Differential diagnosis

- Herpangina
- Herpetic stomatitis
- Erythema multiforme
- Erosive lichen planus
- Pemphigus
- Pemphigoid.

Diagnosis

RAS diagnosis is based on history, clinical

presentation, and histopathology.

Major criteria	Description
Clinical presentation	Solitary or multiple round or oval ulcers, shallow, regular margins, yellow-gray base, surrounded byerythematous margins. Ulcers are never preceded by vesicles.
Recurrence	At least three attacks of RAS within past 3 years, ulcers do not appear in the same focal site
Mechanical hyperalgesia	It is painful lesion,worsens by movement of ulcer affected area.
Self-limitation of condition	Ulcer heals spontaneously without sequelae with or without treatment

Major criteria for diagnosis of minor RAS (Natahet al. 2004)[7]

Minor criteria	Description
Family history of RAS	Positive family history of RAS present
Age of onset	First attack below 40 years
Location	Non-keratinized oral mucosa
Duration	Ulcers lasts from days to few weeks
Pattern of recurrence	Irregular
Histopathological examination	Non-specific inflammation

Minor criteria for diagnosis of minor RAS

Management

There is no absolute curative treatment for RAS. The exact systemic association with RAS must be ruled out, specially in cases where there is abrupt development of ulceration in adulthood. Laboratory investigations such as CBC, red cell folate, serum ferritin levels, and vitamin B12 recommended. Screening for GSE must be done in cases where associated systemic manifestations of GSE are present.[3,18,1920]

Conclusion

RAS is a very common, recurrent painful ulceration occurring in the oral cavity. Etiopathogenesis of this disease is yet debatable. Treatment planning must be directed towards providing Symptomatic relief by reducing pain, increasing the duration of ulcer-free periods, and accelerating ulcer healing.

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