Guidelines for Diagnosis and Treatment of Recurrent Aphthous Stomatitis for Dental Practitioners

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Abstract

Recurrent aphthous stomatitis (RAS) is one of the frequent clinical oral diseases causing painful ulceration in the oral cavity. It is easy to define the clinical features and characteristics of this disease, etiology and pathogenesis remains unclear. As a result, the treatment options are still inadequate with the ability to reduce the duration, healing time, rate of recurrence and conclusive intervention. The review article aims to discuss the pathogenesis, clinical features, different treatment modalities and updates that are currently available and offer the clinician a clear and detailed picture of how to deal with RAS in an appropriate manner.

Key Words: *Recurrent aphthous stomatitis, Ulcer, Topical, Oral disease.*

Introduction

Recurrent aphthous stomatitis (RAS) is considered as the most frequent mucosal lesion occurs in oral cavity[1]. These are described as most often single or multiple, round or ovoid ulcers with yellow floors and surrounded by erythematous haloes[1].It is one of the most common oral ulcerative and vesiculobullous lesion seen in children and adults[2].The classic recurrent aphthous stomatitis presentation is most often, self-limiting ulcers that primarily affect non-keratinized oral mucosa like buccal mucosa, labial mucosa and floor of mouth[2]. Spontaneously the ulcer recover within 7-14 days[2]. These are quite painful which makes it difficult to chew, swallow and speak, hence it has a negative impact on the quality of life of the patient[3]. Aphthous stomatitis is classified into three forms:

1. Minor recurrent aphthous ulcer (Figure 1)
2. Major recurrent aphthous ulcer (Figure 2)
3. Herpetiform ulcer (Figure 3)

It is more prevalent in females[1]. Aphthous ulcers have been recorded from 5% to 66% between different nations[1]. The cause of aphthous ulcer is unclear and many triggers like hormonal changes, injury, medications, food hypersensitivity, dietary deficiency, stress and smoking are still involved in this disease[1].

PREDISPOSING FACTORS[1]:

HORMONAL FACTORS[1]:

During mensturation, premenstrual period, pregnancy, dysmenorrhea

TRAUMA:

Sharp tooth, injury due to tooth brush, site of local anesthetic injection, dental treatment, dental trauma, self-inflicted bites, oral surgical procedures.

DRUGS:

Phenindione, phenobarbital, piroxicam, niflumic acid, sodium hypochlorite, nicorandil, captopril

NSAIDS example: propionic acid, diclofenac, phenylacetic acid

FOOD HYPERSENSITIVITY:

Chocolate, coffee, almonds, cereals, strawberries, tomatoes, cheese, wheat flour

NUTRITIONAL DEFICIENCY:

Vitamin B1, B2, B6 deficiency, anaemia

STRESS:

High levels of psychological stress, acute psychologic problems, anxiety leads to parafunctional habits like lip biting, check biting.

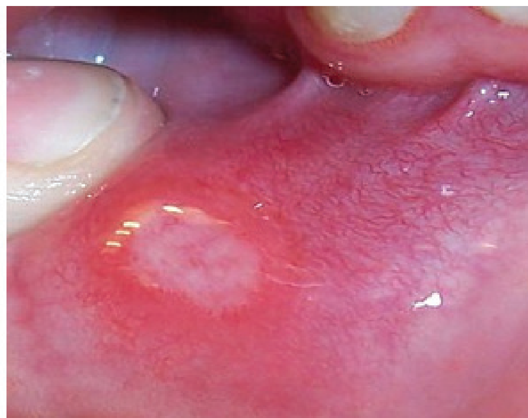

Figure 1: Recurrent aphthous minor

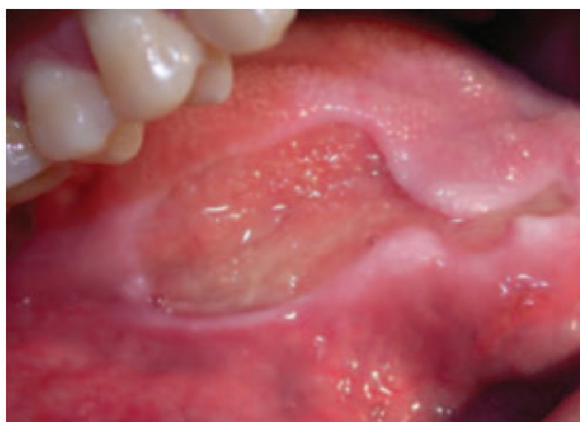

Figure 2: Recurrent apthous major

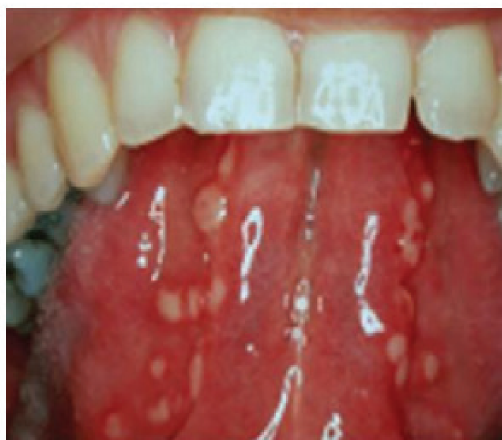

Figure 3: Herptiform ulcer

TOBACCO:

Patients who stop smoking frequently complain of RAS.

INFECTION:

Helicobacter pylori, streptococci, herpes simplex virus, cytomegalovirus, Epstein barr virus, HIV.

HEREDITARY:

For patients with RAS family history, ulcers tend to occur earlier and more severe than those without family history.

SYSTEMIC DISORDERS[6]:

- Behcet's syndrome
- Crohn's disease
- Ulcerative colitis
- Celiac disease
- Cyclic neutropenia
- Gluten sensitive enteropathy
- IgA deficiency
- Immunocompramised conditions
- Inflammatory bowel disease
- Mouth and genital ulcers with inflamed cartilage
- periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis
- Reactive arthritis
- Sweet's syndrome
- Ulcus vulvae acutum

PATHOGENESIS:

Pathogenesis of aphthous ulcer is still unclear.

Patient with recurrent aphthous ulcer have alteration of local cell mediated immunity[3].

ABNORMAL T CELL MEDIATED IMMUNE REACTION

Results in:

Decreased ratio of CD4+ to CD8+[3].

Decreased T-lymphocyte level[3].

Increased levels of T- cell receptor ϒδ+.

Increased Tumor necrosis factor α level[3].

CLINICAL FEATURES[1,2,3,5,6,7]:

MINOR[1,2,3,5,6,7]:

- OTHER NAME : Mikulicz's aphthae
- AGE : 10 and 30 years
- SEX : Female than men
- NUMBER OF ULCER : 1 – 5
- SIZE OF ULCER : <10 mm
- DURATION : 7 – 14 days
- HEAL WITH SCARRING : No
- PERCENTAGE : 85%
- OTHER SYMPTOMS : Burning sensation, pain, erythema.
- SITE : Non- keratinized mucosa particularly labial and buccal mucosa, dorsum and lateral border of tongue

MAJOR[1,2,3,5,6,7]:

- NAME : Sutton's disease/ periadenitis mucosa necrotica recurrens (PNMR)
- AGE : No age predilection
- SEX : Male
- NUMBER OF ULCER : 1 - 3
- SIZE OF ULCER : >10 mm
- DURATION :2 weeks – 2 months
- HEAL WITH SCARRING: yes
- PERCENTAGE : 5-10%
- OTHER SYMPTOMS : Pain, burning sensation, dyaphagia
- SITE : Keratinized and non keratinized mucosa, particularly soft palate

HERPTIFORM[1,2,3,5,6,7]:

- AGE : Third
- SEX : Female
- NUMBER :5 – 20 (upto 100)
- SIZE :1 – 2 mm
- DURATION :7 – 14 days
- HEALING WITH SCARRING: No
- PERCENTAGE :5-10%
- OTHER SYMPTOMS : Reminiscent of herpes simplex infection.

SITE : Non keratinized mucosa but particularly floor of mouth and ventral surface of tongue

DIAGNOSIS:

The correct diagnosis of RAS relies on a detailed and accurate history of the clinic and ulcer evaluation[1].

Following features should be noted from the physicians[1]:

- Important points in history
- Family history
- Number of ulcer
- Size and shape of ulcer
- Site of ulcer
- Frequency of ulcer
- Duration of ulcer
- Edge of ulcer
- Base of ulcer

· Genital ulcer

· Drug allergy

· Dermatological problems

· GIT disturbances

HEMATOLOGICAL FINDINGS:

INVESTIGATIONS TO DO[1]:

· Hemoglobin and complete blood count

· Erythrocyte sedimentation rate/ c- reactive protein

· Serum B12

· Red cell folate

· Anti gliadin and anti endomysial autoantibodies

· Total hematological screening of RAS patients was suggested to identify serum ferritin, iron, folate and vitamin B deficiencies[5]. 11% to 36% of patients with RAS were suffered from deficient levels of serum ferritin or iron[5].

HISTOPATHOLOGIC FINDINGS:

Due to the unspecific nature of the ulcer, a histopathologic specimen is rarely required for the diagnosis of RAS.

FOR MINOR APHTHOUS ULCER[7]:

· Oral mucous membrane shows a fibrinopurulent membrane covering the ulcerated area[7].

· Superficial colonies of micro organisms may also be seen occasionally, in this membrane[7].

· Chronic inflammatory infiltrate seen in connective tissue below the ulcer with considerable necrosis of tissue near the surface of the lesion[7].

· Neutrophils are noticed predominantly beneath the ulcer and lymphocytes prevailing adjacent to this[7].

· Granulation tissue may be seen near the base of the lesion and epithelial proliferation is present at the margins[7].

· The histologic features of oral ulcers in RAS major is identical with RAS minor[7].

CYTOLOGICAL SMEAR FINDINGS:

Changes in the nuclei of epithelial cells taken be cytologic smears from RAS were described.

Anitschkow cells and consists of cells with elongated nuclei containing a linear bar of chromatin extending towards the nuclear membrane with radiating process of chromatin[7].

These are little abundant in patient with RAS but are not pathognomic of the disease[7].

Ultrastructurally, the nuclear chromatin was made up of pleomorphic masses creating an irregular band along the long axis of nucleus rather than being dispersed randomly.[7]

IMMUNOLOGIC FINDINGS: Direct and indirect immunofluorescence studies are not sensitive or precise RAS diagnostic tests and should therefore not be used unless other oral mucosal diseases (e.g., pemphigus and pemphigoid) are excluded[5].

SALIVARY BIOMARKERS:

ETIOLOGY : Stress

SALIVARY BIOMARKERS: Cortisol, Immunoglobulin(Secretory IgA), Lysozyme, Chromogranin A, α amylase.

DIFFERENTIAL DIAGNOSIS:

When treating patients with recurrent aphthae, multiple factors should be included in the differential diagnosis[4]. A primary consideration is that, relative to more severe conditions, benign aphthae tend to be smaller and are more often self-limited[4]. Major aphthae may be correlated with infection with human immunodeficiency virus (HIV)[4].

INFECTION : DIFFERENTIAL DIAGNOSIS[4]:

HERPES SIMPLEX VIRUS : TZANCK stain positive – inclusion bearing giant cells

VARICELLA ZOSTER VIRUS : Clinically have unilateral extra-oral and intra-oral distributing pattern following trigeminal pattern.

COXSACKIE VIRUS : Low grade fever, malaise and will resolve within 7 to 15 days.

Hand, foot, buttock lesions seen in children.

ERYTHEMA MULTIFORME: Seen in both attached and movable mucosa

LICHEN PLANUS : Not always painful

SYPHILIS: Skin lesions other than ulcer, risk factors ,Rapid plasma reagin - positive

fluorescent treponemal antibody absorption test – positive

HISTOPLASMOSIS: Prolonged lesions, immunocompromised patient, culture – positive.

AUTOIMMUNE : DIFFERENTIAL DIAGNOSIS[4]:

BEHCET'S SYNDROME: Ulcer in genital areas, Retinitis, Uveitis

REITER'S SYNDROME: Uveitis is seen, Conjunctivitis, Reactive arthritis

LUPUS ERYTHEMATOSUS : Malar rash also called butterfly rash, Antinuclear antibody test – positive

PEMPHIGUS AND BULLOUS PEMPHIGOID: Involvement of skin

CYCLIC NEUTROPENIA: Fever (periodically), Neutropenia

NEOPLASM: DIFFERENTIATING FINDINGS[4]:

SQUAMOUS CELL CARCINOMA: L o n g duration, Head and neck adenopathy, Biopsy – positive.

TREATMENT:

The RAS etiology is not yet understood. Therefore, there is no consensus in the treatment of RAS, several treatments have been tried, few have been randomized double-blind[2].

GOALS:

The primary goals of RAS therapy are pain management, shorten the duration of ulcer and restore the normal oral function[2].

Secondary objectives are to reduce the frequency and extent of recurrence and to sustain remission[2].

TOPICAL2:

- Pastes / gels
- mouthwashes
- Local anesthetics and analgesics
- Topical corticosteroids and anti-inflammatory agents
- Herbal treatments
- Immunomodulatory agents

PHYSICAL2:

- Silver nitrate
- Laser
- Ultrasound therapy
- excision

SYSTEMIC2:

- Immune and inflammatory suppression
- Immune enhancement
- Biologics
- Other treatment: Diet supplements

The treatment types vary from topical application to clinical drug administration, and even the new ultrasound techniques have been tested2. But the treatment totally depends on the severityof the ulcers and whether the ulcer is associated with any systemic disease2.

FIRST LINE TREATMENT3:

Topical agents like gels, creams or oinment are the first choice of management of recurrent aphthous stomatitis. Topical anti-inflammatory agents are used in primary treatment of RAS lesions

Eg: orabase, mucopain.

TOPICAL:

Antiseptic :Chlorhexidine Gluconate, Triclosan.

Anti-inflammatory/ Analgesic : Benzydamine Hydrochloride, Diclofenac

Anesthetic : Lidocaine, Benzocaine

antibiotic : Chlortetracycline, Doxycycline

Corticosteroids: Hydrocortisone hemisuccinate, Triamcinolone acetonide.

SECOND LINE TREATMENT3:

For patients whose symptoms are not improved by the primary therapy will go for second line therapy.

SYSTEMIC:

Immunomodulator: Levamisole, Colchicine, Thalidomide, Dapsone

Antibiotic : Penicillin G Potassium

Corticosteroids : Prednisone

Conclusion

Recurrent aphthous stomatitis remains a wide spread oral mucosa disorder; its exact etiology remains unclear. RAS treatment tends to be non- specific and observational upto now. Different methods of therapy may be used. In most cases, these modalities can reduce pain and promote recovery, but they are not to improve recurrence rate. Future research should concentrate on defining RAS etiology, establishing a proper RAS diagnostic criteria and definitive treatment and enhancing clinical trial development and monitoring

ReferenceS

1. Tarakji B, Gazal G, Alaizari N et al., Guidelines for diagnosis and treatment of recurrent aphthous stomatitis for dental practioners. J. International oral health 2015; 7 (5): 74-80.
2. Sabbagh A H, Felemban M F. Therapeutic management of recurrent aphthous stomatitis: A review of the growing knowledge. Annals of International Medical and Dental Research 2016; vol 2, issue(6).
3. Sharma D, Garg R. A comprehensive review on aphthous stomatitis, its types, management and treatment available. J Developing Drugs 2018; 7:2.
4. David R. MCBRIDE. Management of aphthous ulcer. Am Fam Physicians 2000; jul1;62(1):149-154.
5. Namrata M, Abilasha R. Recurrent aphthous stomatitis- review. International J.Orofacial biology 2017. Vol 1: Issue 2.
6. Neville, Damm, Allen, Bouquot. Textbook of oral and maxillofacial pathology. 3rd edition.
7. Shafer, Hine, Levy. Shafer's textbook of oral pathology. 8th edition.