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Clinical presentation and predisposing factor of recurrent aphthous stomatitis

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Abstract:

Recurrent Aphthous Stomatitis (RAS) is the most common ulcerative disease affecting the oral mucosa. It occurs mostly in healthy individuals and has atypical clinical presentation in immunocompromised individuals. The etiology of RAS is still unknown, but several local, systemic, immunologic, genetic, allergic, nutritional, and microbial factors, as well as immunosuppressive drugs, have been proposed as causative agents. This review article summarizes the clinical presentation and predisposing factor of recurrent aphthous stomatitis.

Introduction:

Recurrent aphthous stomatitis (RAS) remains the most common ulcerative disease of the oral mucosa presenting as painful round shallow ulcers with well-defined erythematous margin and yellowish-gray pseudomembranous center. RAS has a characteristic prodromal burning sensation that lasts from 2 to 48 hours before an ulcer appears. It occurs in otherwise healthy individuals and is typically located on the buccal and labial mucosa and tongue. Involvement of the heavily keratinized mucosa of the palate and gingiva is less common.

Several factors have been proposed as possible causative agents for RAS. These include local factors, such as trauma in individuals who are genetically susceptible to RAS, microbial factors, nutritional factors, such as deficiency of folate and B-complex vitamins, immunologic factors, psychosocial stress, and allergy to dietary constituents[1]. Extensive research has focused predominantly on immunologic factors, but a definitive etiology of RAS has yet to be clearly established.[1]

Discussion:

Clinical presentation:

RAS is characterized by recurrent bouts of solitary or multiple shallow painful ulcers, at intervals of few months to few days in patients who are otherwise well.[2] RAS has been described under three different clinical variants as classified by Stanley in 1972.[3]

1. Minor RAS is also known as Miculiz's aphthae or mild aphthous ulcers. It is the most common variant, constituting 80% of RAS. Ulcers vary from 8 to 10 mm in size. It is most commonly seen in the nonkeratinized mucosal surfaces like labial mucosa, buccal mucosa, and floor of the mouth. Ulcers heal within 10–14 days without scarring.
2. Major RAS is also known as periadenitis mucosa necrotica recurrens or Sutton's disease. It affects about 10–15% of patients. Ulcers exceed 1 cm in diameter. Most common sites of involvement are lips, soft palate, and fauces. Masticatory mucosa like dorsum of tongue or gingiva may be occasionally involved. The ulcers persist for up to 6 weeks and heal with scarring.
3. Herpetiform ulceration is characterized by recurrent crops of multiple ulcers; may be up to 100 in number. These are small in size, measure 2–3 mm in diameter. Lesions may coalesce to form large irregular ulcers. These ulcers last for about 10–14 days. Unlike herpetic ulcers, these are not preceded by vesicles and do not contain viral infected cells. These are more common in women and have a later age of onset than other clinical variants of RAS.[3]

Predesposing factor:

1. **Genetics** A genetic predisposition for the development of apthous ulcer is strongly suggested as about 40% of patients have a family history and these individuals develop ulcers earlier and are of more severe nature. Various associations with HLA antigens and RAS have been reported. These associations vary with specific racial and ethnic origins.
2. **Trauma** trauma to the oral mucosa due to local anesthetic injections, sharp tooth, dental treatments, and tooth brush injury may predispose to the development of recurrent aphthous ulceration (RAU).
3. **Tobacco** Several studies reveal negative association between cigarette smoking, smokeless tobacco and RAS. Possible explanations given include increased mucosal keratinization; which serves as a mechanical and protective barrier against trauma and microbes. Nicotine is considered to be the protective factor as it stimulates the production of adrenal steroids by its action on the hypothalamic adrenal axis and reduces production of tumor necrosis factor alpha (TNF-α) and interleukins 1 and 6 (IL-1 andIL-6).
4. **Drug** Certain drugs have been associated with development of RAU; these include angiotensin converting enzyme inhibitor captopril, gold salts, nicorandil, phenindione, phenobarbital, and sodium hypochloride. NSAIDS such as propionic acid, diclofenac, and piroxicam may also cause oral ulceration similar to RAS.
5. **Hematinic deficiency** Deficiencies of iron, vitamin B12, and folic acid predispose development of RAS. Deficiencies of these hematinics are twice more common in these individuals than controls. Contrary findings in various studies relating the association of hematinic deficiency and RAS.
6. **Gluten sensitive enteropathy/celiac disease, inflammatory bowel disease** Gluten sensitive enteropathy (GSE) is an autoimmune inflammatory disease of small intestine that is precipitated by the ingestion of gluten, a wheat protein in susceptible individuals. It is characterized by severe malnutrition, anemia, abdominal pain, diarrhea, aphthous oral ulcers, glossitis, and stomatitis.
7. **Sodium lauryl sulfate - containing toothpaste** An increased frequency in the occurrence of RAS has been reported on using sodium lauryl sulfate (SLS)-containing tooth paste with some reduction in ulceration on use of SLS-free tooth paste.
8. **Hormonal changes** Conflicting reports exist regarding association of hormonal changes in women and RAU. Studies state association of oral ulceration with onset of menstruation or in the luteal phase of the menstrual cycle.
9. **Stress** Stress has been emphasized as a causative factor in RAU. It has been proposed that stress may induce trauma to oral soft tissues by parafunctional habits such as lip or cheek biting and this trauma may predispose to ulceration.[2,3]

Micro organisms implicated in apthous ulcers

Several micro organisms have been implicated in the pathogenesis of RAS. Several contrary findings have been reported in the various studies published.

RAS and oral streptococci Oral streptococci have been considered as microbial agents in the pathogenesis of RAS. They have been implicated as microorganisms directly involved in the pathogenesis of these lesions or as agents which serve as antigenic stimuli, which in turn provoke antibody production that cross-react with oral mucosa. It has been suggested that L form of α-hemolytic streptococci, *Streptococcus sanguis*; later identified as *Streptococcus mitis* was the causative agent of this disease.

RAS and Helicobacter pylori *H. pylori* has been implicated as one of the organisms in the etiopathogenesis of RAS. *H. pylori* is a gram-negative, S-shaped bacterium that has been associated with gastritis and in chronically infected duodenal ulcers. *H. pylori* has been reported to be present in high density in dental plaque.

Viruses as etiologic agents in RAS Various viruses have been implicated in the etiopathogenesis of recurrent apthous stomatitis. There have been several suggestive, but as yet there exists inconclusive evidence toward a viral etiology; e.g Varicella zoster, Cytomegalovirus and Epstein-barr virus (EBV).[4]

Conclusion:

RAS is the most common ulcerative disease affecting the oral mucosa. Its etiology is still unknown, occurs mostly in healthy individuals and has a more severe clinical presentation in immunocompromised individuals. Several local, systemic, immunologic, genetic, allergic, nutritional, and microbial factors as well as immunosuppressive drugs have been proposed as causative agents.

References:

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