



## CHRONIC RECURRENT APHTHOSIS STOMATITIS

Radjabov Alisher Islomovich, Ziyaeva Feruza Ravshanovna

Ministry of Internal Affairs, Tashkent. Uzbekistan

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| <p><b>Received:</b> 11<sup>th</sup> November 2022<br/><b>Accepted:</b> 14<sup>th</sup> December 2022<br/><b>Published:</b> 30<sup>th</sup> January 2023</p> | <p>Pathology of the verbal mucosa has a special place among dental diseases because its occurrence and clinical manifestations are regularly related to the influence of numerous local and general causes. The distinctive features of aphthous stomatitis appearance in women of fertile age taking methotrexate were the accessibility of a pronounced painful symptom, a sluggish slowly progressing permanent course, prolonged period of recovery processes extension, and agonizing quality of regional lymph hubs</p> |

**Keywords:** apththa, relapse, stomatitis, ulcer, diseases of the oral cavity, topical therapy, systemic therapy.

**INTRODUCTION.** Recurrent aphthous stomatitis (RAS) remains the most frequent ulcerative disease of the oral mucosa, manifested by painful rounded shallow ulcers with clearly defined erythematous edges and a yellowish-gray pseudomembranous center [1]. RAS has a characteristic prodromal burning sensation that lasts from 2 to 48 hours before the appearance of an ulcer. It occurs in healthy people and is usually localized on the mucous membrane of the cheeks, lips and tongue. The involvement of severely keratinized mucous membranes of the palate and gums is less common. Ulcer attacks can recur at intervals of several months to several days, affecting otherwise healthy people. Aphthous ulcers are usually very painful during the first 4-5 days and can interfere with eating and talking during this period. The first lesions occur in childhood or adolescence, and it is estimated that up to 25% of the world's population is affected by ASD [2, 3]. Lesions are often located at the bottom of the oral cavity and the ventral surface of the tongue. The onset of Hera's is usually later than that of Mira's and Mares, and women are reportedly more susceptible than men.

### Epidemiology

Approximately 20% of the general population is affected by ASD, but the incidence ranges from 5% to 50%. Such a significant difference in estimated prevalence depends on the origin of the studied groups and populations, as well as on the design and methodology of research. The presence of aft directly during medical examination is detected in a smaller percentage of those examined compared to studies based on information collected from patient medical histories. The second decade of life is considered the peak period of the emergence of ASD with the first episode in childhood or later in life. The peak of the occurrence of TIMES occurs at the age of 10 to 19 years and becomes less frequent with age, geographical location or gender [7, 37]. If ASD begins or increases

significantly in severity after the third decade of life and into adulthood, this should increase the suspicion that the cause of the condition may be related to an underlying disease, such as a hematological or immunological anomaly, connective tissue disease or Behcet syndrome.

### Etiopathogenesis

Many trigger factors are involved in the etiopathogenesis of the disease: genetic predisposition, viral and bacterial infections, food allergies, deficiency of vitamins and trace elements, systemic diseases, increased oxidative stress, hormonal disorders, mechanical damage. The role of genetic factors is based on the observation of families suffering from ASD and confirmed by studies of identical twins; the risk of developing the disease in monozygotic twins is higher than in dizygotic twins [6, 35]. No consistent relationship has been demonstrated between specific HLA and RAS haplotypes [7].

### Hematite insufficiency

20% of patients with ASD have a deficiency of hematin (iron, folic acid, vitamin B12) [8]; however, it has been proven that the addition of missing trace elements affects the course of the disease in very few cases [9].

### Food allergies

According to some researchers, some food ingredients (chocolate, gluten, cow's milk, nuts), preservatives and food dyes can cause a pro-inflammatory cascade, and in some patients clinical improvements were observed after the introduction of an elimination diet. However, these conclusions were not confirmed by subsequent studies [11].

### Mechanical injuries

In many patients, lesions may appear soon after mechanical irritation of the area. The mechanism of this reaction remains unknown [12].

### Systemic diseases and hormonal imbalance

The most well-known medical disorder associated with ASD is Behcet syndrome. Recurrent apththae occur



more often in patients with gastrointestinal disorders, mainly from the group of chronic inflammatory bowel diseases [2]. This correlation may partly be a consequence of a lack of food and trace elements or be associated with autoimmune reactions. Exacerbation of ASD is observed in the luteal phase of the menstrual cycle and during menopause, while remission, apparently, often occurs during pregnancy and in women taking contraceptives [11].

### **Microbial infections**

The role of many viruses and bacteria has been emphasized to support the infectious etiology of ASD. However, numerous studies have not provided evidence. Oral streptococcus colonizes aphthous ulcers, and it has been suggested that it can cross-react with mitochondrial proteins, causing damage to the oral mucosa [13]. Meta-analysis supports the link between RAZ and *Helicobacter pylori* infection, the presence of bacteria in the foci of RAZ causes controversy.

### **Stress**

It is believed that stressful events aggravate ASD, affect its duration or cause the onset of the disease [2].

### **Mucosal and salivary microbiota**

It is estimated that the human oral cavity is colonized by about 700 different major bacterial species that produce a huge number of different peptides and polysaccharides of molecular type associated with pathogens that can interact with each other and the host immune system to maintain a stable symbiotic microenvironment during health [15]. If this balance is disturbed, the symbiotic relationship shifts, allowing potentially pathogenic species to colonize or overgrow, causing a pathogenetic process leading to symptoms associated with various diseases [16]. In general, nine main types of bacteria live in the mouth of a healthy person [17]. At the level of the genus, *Streptococcus* is known to be the most common genus.

### **Clinical manifestation and pathogenesis**

Patients with ASD usually experience prodromal burning sensations that last from 2 to 48 hours before the appearance of an ulcer. The ulcers are rounded, with well-defined erythematous edges and a shallow ulcerated center, covered with a yellowish-gray fibrinous pseudomembrane. Ulcers usually develop on the non-corneating mucous membrane of the oral cavity, with the most frequent localizations being the mucous membrane of the cheeks and lips, and persist for about 10 to 14 days without scarring (see Table 1). Ulcers in the oral cavity observed in Behcet's disease are clinically similar, but more often represent large aphthae [18]. Microscopic characteristics of ulcers are non-specific. The pre-ulcer lesion demonstrates subepithelial inflammatory mononuclears with

abundant mast cells, connective tissue edema and lining of the edges with neutrophils [19]. Epithelial damage usually begins in the basal layer and spreads through the surface layers, which eventually leads to ulceration and superficial exudation. The presence of extravascular erythrocytes around the edge of the ulcer, subepithelial extravascular neutrophils, numerous macrophages loaded with phagolysosomes, and nonspecific binding of the cells of the spiny layer with immunoglobulins and complements may be the result of leakage from the vessels and passive diffusion of serum proteins. These data suggest that the pathogenesis of ASD may be mediated by immunocomplex vasculitis [20, 39]. The onset of ASD damage is associated with a cell-mediated immune response, T-cell formation and TNF- $\alpha$  production. It is shown that the peripheral blood mononuclear cells of patients with ASD secrete a large amount of TNF- $\alpha$ , indicating that TNF- $\alpha$  plays a key role in the pathogenesis of ASD. [21-23]. Consequently, TNF- $\alpha$ -mediated adhesion of endothelial cells and neutrophil chemotaxis initiate a cascade of inflammatory processes leading to ulceration [25]. Most TNF- $\alpha$  is produced in response to the activation of toll-like receptors (TLR), a set of functional membrane receptors associated with the immune response and protection of the epithelial barrier. TLRs have both pro-inflammatory and anti-inflammatory properties. Taking into account that in some patients it was found that pro-inflammatory TLRs were significantly increased in the epithelium and own plate of ASD lesions, [27] a decrease in the level of TLR expression with anti-inflammatory activity was also found in another group of patients with ASD [30]. Thus, the role of TLR in the pathogenesis of ASD still needs to be more precisely determined, but it is possible that an imbalance in the pro-inflammatory and anti-inflammatory activity of TLR may increase susceptibility to RAS in some people.

### **Therapy**

Therapeutic goals include reducing the pain of ulcers, accelerating the healing of ulcers and preventing relapses [33-36]. Local therapy and anesthetics such as lidocaine and benzocaine are used for short-term pain relief, especially in the case of large ulcers. Corticosteroids are often used to accelerate the healing of ulcers and reduce the symptoms of ASD. Preference is given to a potent steroid (dexamethasone, triamcinolone, fluciclonide and clomezol) in mouthwashes. Although there is no evidence of bacterial origin of ASD, topical antimicrobials such as chlorhexidine, tetracycline and dilute hydrogen peroxide are associated with accelerated healing of ASD ulcers. It has been shown that drugs with antimicrobial, anti-inflammatory and analgesic effects cause some positive



effects when used as a mouthwash. Of secondary importance are coating agents that protect and strengthen the natural barrier of the mucous membrane: sucralfate, bismuth subsalicylate, bioadhesive agents for oral use.

Particularly severe cases of ASD are treated with systemic therapy: systemic steroids, colchicine, thalidomide:

— systemic steroids: short course. Systemic steroids can sometimes be used to treat a particularly severe episode of extensive ASD;

— colchicine: at a dose of 0.6-1.2 mg / day. showed encouraging results in reducing the number and duration of aphthous lesions;

— thalidomide: controlled trials have demonstrated the efficacy of thalidomide in the treatment of ASD, causing complete remission or significant improvement in most patients.

The use of lasers (CO<sub>2</sub>, ND:YAG, diode laser) to relieve symptoms and accelerate the healing of RA is a therapeutic option.

#### **LITERATURE:**

1. Aliyev N.H. Chaka pastki zha Kurgan no articular pathology diagnostic method / / medicine and sport – Samarkand, 2020/3. 59-62 rate.
2. Aliyev N.H. Gafforov S.A., Idiev G.E. How-low level of impact of regulatory legislation and pathology of mechanisms based on tamoillaries. Tibbietta Yang kun. -2020. - No. 1. pp. 132-135
3. N.H Aliyev, S.A Gafforov, G.E Idiev. Scientific and practical substantiation of changes in the function of work of the lower-fast joint in norm and pathology // New day in medicine. 2020.No.-1. p.132-135
4. Aliev Navruz Khasanovich. Correction of Internal Disorders of the Temporomandibular Joint Using Muscle Relaxation Splints Made With Cad/Cam Technologies // 2022.10.28. Vol. 1 – p. 160-166.
5. Tappuni AR, Kovacevic T, Shirlaw PJ, Challacombe SJ. Clinical assessment of disease severity in recurrent aphtous stomatitis. J Oral Pathol Med 2013;42:635-41.
6. Giannetti L, Murri dello Diago A, Lo Muzio L. Recurrent aphtous stomatitis. Minerva Stomatol 2018; 67:125-8. DOI: 10.23736/S0026-4970.18.04137-7.
7. Yilman S, Cimen KA. Familial Behçet disease. Rheumatol Int 2010;30:1107-9.
8. Albanidou-farmaki E, Deligiannidis A, Markopoulos AK, Katsares V, Farmakis K, Parapanissiou E. HLA aplotypes in recurrent aphtous stomatitis: a mode of inheritance? Int J Immunogenet 2008;35:427-32.
9. Khan NF, Saeed M, Chaudhary S, Khan NF. Haematological parameters and recurrent aphtous stomatitis. J Coll Physicians Surg Pak 2013;23:124-7.
10. Lalla RV, Choquette LE, Feinn RS, Zawistowski H, Latortue MC, Kelly E,T et al. Multivitamin therapy for recurrent aphtous stomatitis: a randomized, double-masked, placebo-controlled trial. J Am Dent Assoc 2012;7:370-6.
11. Akintoye SO, Greenberg MS. Recurrent aphtous stomatitis. Dent Clin N Am 2005;49:31–47.
12. Tarakji B, Baroudi K, Kharma Y. The effect of dietary habits on the development of the recurrent aphtous stomatitis. Niger Med J 2012;53:9-11.
13. Natah SS, Konttineen YT, Enattah NS, Ashammakhi N, Sharkey KA, Häyriinen-Immonen R. Recurrent aphtous ulcers today: a review of growing knowledge. Int J Oral Maxillofac Surg 2004;33:221-34.
14. Riggio MP, Lennon A, Ghodrathnama F, Wray D. Lack of association between Streptococcus oralis and rcurrent apytous stomatitis. J Oral Pathol Med 2000;29:26-32.
15. Gafforov S.A., Aliev N.H. Improvement of diagnostic methods and treatment of parafunction of chewable Muscles in pain syndromes of a High-Lower jaund joint // Journal of Advanced Research in Dynamical and Control Systems. ISSN: 1943-023X. Volume 12,07- special issue. -P.2102-2110. 2020
16. Paster BJ, Boches SG, Galvin JL, Ericson RE, Lau CN, Levanos VA, et al. Bacterial diversity in Human subgingival Plaque. J Bacteriology 2001;183:3770-83.
17. Doktor MJ, Paster BJ, Abramowicz S, Ingram J, Wang YE, Correll M, et al. Alterations in diversity of the oral microbiome in pediatric bowel disease. Inflamm Bowel Dis 2012;61:935-42.
18. Bik EM, Long CD, Armitage GC, Loomer P, Emerson J, Mongodin EF, et al. Bacterial diversity in the oral cavity of 10 healthy individuals. ISME J 2010;4:962-74.
19. Oh SH, Han EC, Lee JH, et al. Comparison of the clinical features of recurrent aphtous



- stomatitis and Behcet's disease. *Clin Exp Dermatol* 2009;34(6): e208–12.
20. Woo SB, Greenberg MS. Ulcerative, vesicular and bullous lesions. In: Greenberg MS, Glick M, Ship JA, editors. *Burket's oral medicine*. 11th edition. Hamilton (Canada): BC Decker; 2008. p. 41–76.
  21. Jurge S, Kuffer R, Scully C, et al. Mucosal disease series. Number VI. Recurrent aphthous stomatitis. *Oral Dis* 2006;12(1):1–21.
  22. Lewkowicz N, Lewkowicz P, Dzitko K, et al. Dysfunction of CD41CD25 high T regulatory cells in patients with recurrent aphthous stomatitis. *J Oral Pathol Med* 2008;37(8):454–61.
  23. Lewkowicz N, Kur B, Kurnatowska A, et al. Expression of Th1/Th2/Th3/ Th17-related genes in recurrent aphthous ulcers. *Arch Immunol Ther Exp (Warsz)* 2011;59(5):399–406.
  24. Lewkowicz N, Lewkowicz P, Banasik M, et al. Predominance of Type 1 cytokines and decreased number of CD4(1)CD25(1high) T regulatory cells in peripheral blood of patients with recurrent aphthous ulcerations. *Immunol Lett* 2005;99(1):57–62.
  25. Alimova, N. P., & Asadova, N. H. (2020). The study of anatomy through problem-based learning among medical students. In *The Collection of materials of the international online educational conference "The current state of medical education: problems and prospects* (pp. 138-139).
  26. Natah SS, Hayrinen-Immonen R, Hietanen J, et al. Increased density of lymphocytes bearing gamma/delta T-cell receptors in recurrent aphthous ulceration (RAU). *Int J Oral Maxillofac Surg* 2000;29(5):375–80.
  27. Jumaev A. X. (2021). METHOD FOR ASSESSING THE STATE OF THE ORAL MUCOSA IN DENTAL DEFECTS. *UZBEK MEDICAL JOURNAL*, 2(2).
  28. Hietanen J, Hayrinen-Immonen R, Al-Samadi A, et al. Recurrent aphthous ulcers—a Toll-like receptor-mediated disease. *J Oral Pathol Med* 2012;41(2):158–64.
  28. Akbarov A.N. and Dzhumaev A. (2020). Hygienic condition of dentures in patients with partially removable dentures. *PalArch Journal of Egyptian Archaeology/Egyptology*, 17(6), 14351-14357.