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Etiology of Stomatitis in Patients with Removable Denture

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Abstract:

This literature review focuses on studying the etiological factors contributing to the occurrence of denture stomatitis. Denture stomatitis refers to various inflammatory pathologies of the oral mucosa caused by the dental prostheses in the oral cavity. According to Gavrilov, this term reflects the primary content of the mucosal reaction of saddle and its cause, the dental prosthesis. Since this inflammatory process occurs in 15% to 70% of wearers of complete or partially removable dentures, knowledge of the etiological factors is highly relevant.

Keywords: denture stomatitis, removable denture, oral mucosa.

Introduction. Studies conducted on edentulous individuals have shown that between 15% and 70% of denture wearers develop stomatitis related to their removable denture [1]. The prevalence of this pathology is higher among hospitalized elderly individuals [2,8], smokers [3], and people with comorbidities such as diabetes [4]. Below are some possible etiological factors leading to denture stomatitis. Poor denture maintenance leads to the accumulation of biofilm, colonization of the denture surface with over 1011 microorganisms (bacteria, fungi, viruses) per gram of dry weight [10,11]. Denture stomatitis is considered an infectious disease, differentiating it from sterile inflammation characterized by mechanical stress on the denture [5] and imbalance of the oral cavity's microbial flora or dysbiosis [6]. Denture wearers have a less diverse oral microbiome compared to patients with natural teeth. This is reflected in the abundance of opportunistic pathogens, such as C. albicans. Additionally, C. albicans can penetrate the denture material, thereby forming a microbial reservoir [7,8]. Its primary location is the posterior part of the tongue and other oral cavity sites, such as the mucous membrane, while the film covering the tooth surface is colonized secondarily [9].

The denture in the oral cavity creates ecological niches in which C. albicans tend to form biofilms due to their plasticity, adapting to the host's main regulatory network [12]. Candida selects its bacterial coexistence; thus, the acidity of its environment is favorable for bacilli (streptococci and lactobacilli) but unfavorable for classes of fusobacteria, bacteroides, and flavobacteria, which poorly tolerate acidity [13].

The pathogenesis of candidal denture stomatitis is complex and multifactorial. It involves local and systemic factors related to the host and Candida's ability to adhere and proliferate in the host's epithelial tissues [14,23]. It is important to pay attention to systemic factors in the development of this pathology. Among these factors are diabetes, xerostomia, nutrient deficiencies, and kidney damage. The first factor is diabetes; in this etiological factor, the saliva of diabetics promotes the growth of C. albicans in vitro, and it has been shown that diabetic denture wearers have a higher number of yeast colonies on the surfaces of their dentures compared to non-diabetic individuals [7,15]. The next factor is the influence of systemic nutrient deficiency. Some authors report that anemia and high levels of cholesterol in the blood may exacerbate the course of prosthetic stomatitis [16].

Many studies have shown that kidney damage can also lead to this type of stomatitis, which is often common in elderly individuals. Repeated treatment with antibiotics and sulfonamides may be a predisposing factor due to the microbial changes they cause in the oral cavity[17].

Qualitative and quantitative changes in salivary secretion in elderly patients are likely secondary to the intake of medications, primarily antihypertensive drugs, rather than primary functional deficits. It has been shown that such a decrease acts as a predisposing factor to the virulence of C. albicans species, which is a microbial cause of prosthetic stomatitis[18].

In addition to systemic etiological factors, attention should also be paid to local factors. Local factors include oral cavity traumas, composition of saliva, pH balance of the oral cavity, permeability of acrylic resins, and presence of microbial plaque. Traumas to the oral cavity from improperly fabricated complete or partial removable prostheses can influence the course of inflammation in various ways. A recent study showed that trauma itself does not induce a picture of generalized denture stomatitis but rather may be the cause of localized forms. Instead, in generalized forms, Candida albicans plays the primary pathogenetic role. In this case, trauma may act as a contributing factor that promotes yeast adhesion and penetration, increases epithelial permeability to toxins and soluble substances produced by Candida yeast. Trauma from unstable dentures is also one of the etiological factors of denture stomatitis. Immunohistochemical analysis of the mucosal tissue affected by prosthetic stomatitis demonstrated a possible role of trauma in altering the expression of basement membrane antigens [19].

In addition to trauma, the composition of saliva also plays a role in the development of this pathology. The role of saliva in the colonization of C. albicans remains controversial. Some studies have shown that saliva reduces the adhesion of C. albicans. In fact, saliva contains protective molecules such as lysozyme, lactoferrin, calprotectin, IgA, which reduce the adhesion of Candida to oral cavity surfaces [20]. Other studies have shown that saliva proteins, such as mucins and statherins, can act as adhesion receptors used by mannoproteins present in Candida species. Reduction or complete absence of saliva in individuals with xerostomia leads to changes and imbalance in normal microbial communities, promoting the proliferation of bacteria such as Staphylococcus aureus, which inhibits the normal adaptation of commensals [9]. Additionally, the presence of a low pH level and high oxygen tension reduces the growth of some commensals and increases the proliferation of species such as C., Streptococcus mutans, and Lactobacillus. A recent study showed that saliva plays a dual role in the adhesion of C. albicans to the plastic material used to make dentures: reducing the adhesion of germinated cells and enhancing the adhesion of yeast cells [21]. A low pH level can contribute to the adhesion and proliferation of Candida yeast. In fact,

a pH of 3 is optimal not only for yeast adhesion but also for the enzymatic activity of proteases, which along with lipases are important virulence factors of Candida due to their cytotoxic and cytolitic action. Moreover, high levels of carbohydrates present in saliva can act as an additional source of nutrients for Candida yeast, which, by metabolizing these sugars, produce acidic metabolic products and contribute to maintaining a low pH level in the surrounding environment [9].

Initially, Candida adhesion depends on the micro-porosity of the prosthesis surface [22]. Such surface roughness enables yeast colonization and hinders the destruction of bacteria by mechanical and chemical hygiene measures; therefore, with poor oral hygiene, Candida can penetrate, adhere, and aggregate with bacterial communities such as Streptococcus sanguis, Streptococcus gordonii, Streptococcus oralis, and Streptococcus anginosus (S. milleri) through interactions between proteins and carbohydrates [9]. Various microbiological studies have shown that plaque accumulated on dentures during stomatitis has a complex composition, primarily consisting of gram-positive bacteria [9], such as Streptococcus sanguis, S. gordonii, S. oralis, S. anginosus, staphylococci, and rods. Actinomyces predominate, followed by lactobacilli. Microorganisms present in the oral cavity interact with each other in various ways, both directly using products of their own metabolism and exchanging molecular signals. Several studies have shown that coaggregation involves protein-carbohydrate interactions. It has been demonstrated that Candida is the predominant pathogen in denture stomatitis. Firstly, patients with denture stomatitis exhibit a higher presence of Candida compared to the control group. Secondly, the response of patients to antifungal therapy is characterized by a significant reduction in the number of colonies present in denture plaque. Thirdly, it is important to note that the mass of a yeast cell is 50 times greater than that of a cocci, and the mass of hyphae can be hundreds of times greater than that of a rod. Thus, Candida plays a pivotal pathogenetic role in the development of denture stomatitis, although the concurrent role of bacterial plaque on the prosthesis should not be disregarded [20].

- Pathogenetic Theory

The presence of bacteria such as streptococci and actinomycetes stimulates the body to produce proteases, such as IgA1, and enzymes such as aminopeptidases, hyaluronidases, chondroitinases, and neuraminidases, capable of damaging the epithelium of the oral cavity. These harmful products, remaining in close contact with the oral mucosa, lead to an increase in inflammatory exudate, which promotes not only bacterial colonization but also yeast proliferation, as Candida more easily colonizes the mucous membrane in contact with the surface of the dental prosthesis compared to other parts of the cheek mucosa. Proteases can enhance the pathogenic potential of bacterial substances, leading to the destruction of salivary immunoglobulins. The immune system's response to plaque deposits is responsible for inflammatory lesions. Experimental data have shown that the delayed hypersensitivity reaction to Candida albicans significantly contributes to the inflammatory response and that a typical characteristic of denture stomatitis is the detachment of epithelial cells, leading to epithelial atrophy, rather than hyphal invasion [23]. Treatment of candidal denture stomatitis is challenging due to its multifactorial etiology [24]. The current therapeutic strategy still involves the use of local and systemic antifungal agents, the use of preservatives and disinfectants, microwave irradiation, as well as meticulous removal and control of plaque formation on the denture and oral mucosa.

- Treatment with Antifungal Agents

The most commonly used antifungal agents are antifungal suspensions based on nystatin, amphotericin B, miconazole, and fluconazole. Almost all medications typically induce complete symptom remission within 12-14 days.

Researchers have demonstrated the importance of antifungal therapy in the treatment and prevention of oral candidiasis [24]. They noted that nystatin and amphotericin B, due to their

binding to ergosterol on the cell membranes of Candida, induce changes in cell membrane permeability, leading to their penetration into cells and ultimately their death. Other researchers [25] have provided data indicating that sublethal doses of amphotericin B inhibit Candida adhesion to mammalian cell cultures and that blastospores in the active growth stage are more sensitive to the drug. Other studies have shown that subinhibitory doses of nystatin, amphotericin B, and miconazole inhibit Candida adhesion to epithelial cells [25]. Among the locally applied antifungal agents, the efficacy of "Locetar" has been noted [26]; it is used in the treatment of onychomycosis. Amorolfine belongs to a new class of chemical antifungal agents. Its fungistatic and fungicidal effects are based on changes in the membranes of fungal cells, particularly at the level of sterol biosynthesis. This reduces the content of ergosterol while simultaneously accumulating atypical flat sterols.

- Treatment with preservatives and disinfectants

The use of antiseptic agents, such as a 0.2% solution of chlorhexidine gluconate, administered 3 or 4 times a day, can lead to a significant reduction in plaques but does not have a significant impact on reducing Candida colonies [24]. More encouraging results are obtained when dentures are immersed in a 2% solution of chlorhexidine as an adjunct to local therapy. It is important to note that chlorhexidine should never be prescribed simultaneously with nystatin, as it suppresses antifungal activity. Another antiseptic agent is sodium hypochlorite. It has been proven that immersing the denture in a 0.02% solution of sodium hypochlorite effectively reduces the amount of Candida and bacteria on the denture surface. Unfortunately, sodium hypochlorite cannot be used indefinitely due to its ability to damage handcrafted products [27].

- Microwave Therapy

Microwave irradiation has been proposed as a fast, effective, and inexpensive method for disinfecting dentures. In vitro exposure to microwaves could result in the death of Candida albicans cells. Clinical evaluation has demonstrated the real effectiveness of this method for disinfecting dentures and treating candidal denture stomatitis [28] by subjecting the denture to microwave radiation (350 W, 2450 MHz) for 6 minutes, which removes Candida and bacteria. However, this treatment induces conformational changes in the denture depending on the duration of treatment, thus affecting the feasibility of using this method in conjunction with oral hygiene maneuvers and denture care. In fact, according to quantum theory, the formation of waves leads to the generation of energy, which can affect the dimensional stability of the denture [29].

Conclusions. Denture stomatitis associated with candidiasis remains the most common form of candidiasis in the oral cavity (25-65%), especially among denture wearers, with the primary localization on the palate mucosa. Among the local factors contributing to this condition, the main one is the accumulation of microbial plaque on the surface of the prosthesis, which comes into contact with the mucous membrane. Even if candidal denture stomatitis is asymptomatic, it should be treated because it can serve as a source for more serious infections and contribute to alveolar bone resorption. Destroying and controlling microbial plaque is a more effective approach in therapy and prevention.

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