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Features of Morphological Changes in the Mouth Mucosa in Coronavirus Infection

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ABSTRACT
In connection with the spread of a new coronavirus infection, the number of diseases of the oral mucosa caused by COVID-19 is steadily increasing. It was determined that even with a mild form of the disease with a new coronavirus infection, the proportion of damage to the oral mucosa is high. The results of the analysis of literature data on morphological changes in the oral mucosa during coronavirus infection are presented.

Introduction

COVID-19 (abbreviation for COronaVIrus Disease 2019) is an extremely severe acute respiratory infection caused by the SARS-CoV-2 coronavirus. The SARS-CoV-2 virus is distinguished by its ability to infect various organs both through direct infection and through the body's immune response. This disease downstream can occur both in mild and severe form. One of the frequent complications is the development of viral pneumonia. Coronavirus can also infect the oral mucosa. The pathogenic agent enters the body due to angiotensin-converting enzyme 2, which is localized both on the surface of the alveoli and lung structures, and on the epithelial cells of the oral cavity, where it begins to actively multiply [5].

The oral cavity is the initial section of the digestive tract. SARS-CoV-2 infection can cause changes in the organs and tissues of the oral cavity, which is associated with a wide distribution of ACE2 in the oral cavity, mainly in epithelial cells of the oral mucosa, gums, and fibroblasts of the periodontal ligament [2, 3]. Thus, the oral mucosa is susceptible to SARS-CoV-2 infection and can be an entry gate for the virus [2, 4–8] and also serve as a reservoir for SARS-CoV-2 [9]. In a systematic review of French authors [7], it is noted that a number of molecules (ACE2, furin, cathepsin L, the enzyme of the transmembrane protease SS2 - TMPRSS2 and some others), the high content of which is observed in periodontal tissues, especially in patients with chronic pathology, may be involved in the mechanism of penetration

of SARS-CoV-2 into cells. A number of studies [4, 7] indicate the possible involvement of pro-inflammatory molecules (furin and cathepsin L) in the penetration of the virus into the body, which are released during the development of periodontitis. Researchers from Mexico analyzed the presence of SARS-CoV-2 and its entry factors (ACE2, transmembrane serine proteases – TMPRSS and furin) in a systematic review, and their results show that SARS-CoV-2 can infect a wide range of oral tissues and cells. [10]. Indian researchers detected SARS-CoV-2 in gingival fluid and found that its level correlated with virus isolation from saliva samples and nasopharyngeal swabs [11]. Another Indian study [12] indicates that the sensitivity of gingival fluid to detect SARS-CoV-2 (63.64%) is comparable to that of saliva (64.52%). In addition, Italian [13] and Brazilian [14] researchers identified SARS-CoV-2 in tartar and plaque samples. Thus, we can assume a cumulative viral load in the oral cavity [12, 15].

Features of the morphological structures of the oral mucosa. The oral cavity is called a mirror, which reflects the general state of the body. It represents the initial section of the gastrointestinal tract, where the mechanical processing of food and the formation of a food bolus take place. Like all parts of the gastrointestinal tract, the oral cavity is lined with a mucous membrane, which is covered with stratified squamous epithelium [25, 164,181]. The mucous membrane of the mouth, performing many functions, the main of which are protective, sensitive, suction and plastic. It is a kind of selective semi-permeable barrier and at the same time has a high permeability for the absorption of various substances and drugs, but remains impermeable to most microorganisms. The COR contains numerous receptors that capture various types of stimuli (tactile, temperature, taste, pain). It is a kind of powerful reflexogenic field that has a direct impact on the function of various parts of the gastrointestinal tract [58, 61]. According to the structure in the oral mucosa, epithelium, lamina propria and submucosa can be distinguished, and the thickness of these layers is different in different areas. There is no muscle plate between its own layer and the submucosa in the composition of the COR, which is the main difference in structure from other mucous membranes of the body [72]. The thickest epithelial layer is in the mucous membrane of the hard palate, tongue and gums. The lamina propria is most pronounced in the mucous membrane of the lips, cheeks and gums. The submucosa is well expressed in the area of transitional folds and the floor of the mouth [12, 39]. Normally, the COP epithelium does not keratinize and on the lips, cheeks, and soft palate it consists of the basal and prickly layers. In pathological processes on the hard palate and gums, the epithelium can become keratinized, so the granular and stratum corneum appear in its structure [23]. The barrier properties of the mucous membrane are represented by several processes: regeneration (continuous formation of new cells), cell differentiation (change in morphological and functional properties in the process of displacement to the overlying layers of the mucous membrane) and desquamation (removal of damaged cells or cells containing microorganisms from the surface of the epithelium) [58, 61] . The mucous membrane of the mouth, lips, cheeks contains a lot of nerve fibers and their endings. These are afferent sensory fibers that are associated with the central nervous system and are part of the trigeminal, vagus, facial and glossopharyngeal nerves. Nerve fibers in the papillary layer of the connective tissue plate form a subepithelial plexus [49]. From the branches of this plexus, free and encapsulated nerve endings are formed. The above described features of innervation explain the pronounced pain syndrome in various lesions of the oral mucosa [39, 72]. The blood supply of the oral mucosa also has a number of features: the blood vessels have a fenestrated epithelium, the capillaries of the cheeks have a continuous lining. The veins follow the course of the arterial bed [12]. The lymphatic system of the COP is represented by lymphatic capillaries,

blindly beginning at the tops of the connective tissue papillae. They form lymphatic vessels that run along the course of the blood vessels and carry lymph to the cervical and submandibular lymph nodes [39, 58, 72]. Thus, due to the complex structure of blood supply, innervation, and lymphatic outflow, COR has a wide range of possible adequate responses to stimuli under normal and pathological conditions [12, 22].

A systematic review [16] noted that the most common clinical manifestations in the oral cavity in patients with COVID-19 include taste disturbances, ulcers, wheals, necrotizing gingivitis, opportunistic co-infections, salivary gland changes, white and erythematous plaques. As a rule, lesions from the oral cavity appear simultaneously with the loss of smell and taste. Numerous reports indicate necrotic/ulcerative gums, oral blisters, and overgrowth of opportunistic oral pathogens. SARS-CoV-2 exhibits a tropism for endothelial cells, and COVID-19 mediated endothelitis may not only promote inflammation in oral tissues but also contribute to the spread of the virus. In addition, elevated levels of pro-inflammatory mediators in patients with COVID-19 and oral infectious diseases may disrupt tissue homeostasis and cause delayed disease resolution. This suggests a potential interaction of immune-mediated pathways underlying the pathogenesis of oral organ and tissue changes. Several reports note recurrent herpetic lesions and higher bacterial growth in COVID-19 patients, suggesting an interaction between SARS-CoV-2 and oral virus/bacteria [16]. A review article by Iranian authors [17] notes that dysgeusia is the first recognized oral symptom of a novel coronavirus infection (COVID-19). Oral manifestations of COVID-19 included ulcers, erosions, bullae, vesicles, pustules, tongue with or without fissured papillae, macules, papules, plaques, pigmentation, halitosis, whitish patches, hemorrhagic crusts, necrosis, petechiae, edema, erythema, and spontaneous bleeding. The most common lesions, in descending order, were the tongue (38%), lip mucosa (26%), and palate (22%). The most common diagnoses include aphthous stomatitis, herpetiform lesions, candidiasis, vasculitis, Kawasaki-like syndrome, mucositis, drug rash, necrotizing periodontitis, angular cheilitis, atypical Sweet's syndrome, and Melkersson-Rosenthal syndrome. Oral lesions were symptomatic in 68% of cases, almost the same in both sexes (49% of women and 51% of men). In older patients and with higher severity of COVID-19 disease, oral involvement was more common and severe. According to Iranian authors [17], lack of oral hygiene, opportunistic infections, stress, immunosuppression, vasculitis, and hyperinflammatory response secondary to COVID-19 are the most important predisposing factors for oral lesions in patients with COVID-19. American researchers [18] note that the direct impact of COVID-19 on oral health includes ageusia (the official symptom of COVID-19), which is transient, as well as vesiculobullous mucosal lesions and necrotizing periodontitis. Spanish scientists also point to a high frequency of vesiculobullous lesions of the oral mucosa associated with SARS-CoV-2 infection [19]. A systematic review by scientists from Mexico [20] showed that the initial signs/symptoms after infection with SARS-CoV-2 were dysgeusia, dry mouth and burning mouth, and the main signs/symptoms were the presence of ulcerative lesions, dysgeusia and Candida albicans infection.

A review by scientists from Pakistan [21] discusses various oral manifestations of COVID-19, which included taste disturbance, oral mucosal changes (petechiae, ulcers, plaques, herpes simplex virus type 1 reactivation, geographic tongue, and desquamative gingivitis), and dryness. in the mouth. The most characteristic sites of mucosal lesions are the tongue, palate, and mucosa of the lips. Another Iranian review [22] noted that the most common oral manifestation in COVID-19 was dry mouth, followed by dysgeusia and pseudomembranous oral candidiasis.

Other common symptoms included tongue sensitivity and ulceration, muscle pain during chewing, oral edema, and herpetic lesions. A review by Indonesian authors [23] indicated that oral symptoms associated with SARS-CoV-2 infection included dysgeusia, ageusia, burning sensation in the mouth, dry mouth, and severe halitosis. Oral mucosal lesions ranged from ulceration and depapilation to pseudomembranous macules, nodules, and plaques. Mucosal lesions associated with skin lesions have been observed in the form of crusted lips, multiple ulcerations and rashes, punctate lesions, wheals, and vesiculobullous lesions. The authors note that the resulting oral mucosal lesions mimic herpes zoster infection, herpes simplex virus infection, varicella and foot-and-mouth disease, and oral mucosal lesions with skin manifestations (eg, erythema multiforme).

The results of a survey of people who have had COVID-19 substantiate the need for a dental examination of these patients after their clinical recovery. This will contribute to the timely detection of developed changes in the oral cavity, which can appear both during infection with the COVID-19 virus and in the post-COVID period as a complication of this disease. Dentists have an important task: to detect changes in time, conduct differential diagnostics and prescribe the most correct algorithm for treatment and prevention. Even in young people, in whom the coronavirus infection is predominantly mild, there may be manifestations in the oral cavity that reduce the quality of life and health and, without timely treatment, lead to serious consequences.

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