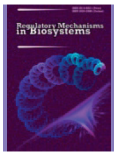

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Candida albicans colonization of the mucous membrane in acute manifestations of COVID-associated oral candidasis

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The study of long-term COVID-19 has become increasingly relevant in recent years and is becoming a priority in modern dentistry. The article presents the results of a study of COVID-associated oral candidiasis in patients with a post-COVID-19 condition. An important fact is that the change in the clinical course of acute oral candidiasis in patients with post-COVID-19 condition, in particular, acute pseudomembranous and acute erythematous candidiasis, is associated with the morphological transformation of *Candida albicans*. We are the first to observe the transformation of *C. albicans* from a yeast-like to a fungal form in patients with COVID-associated oral candidiasis, although the possibility of such transformation in vitro has been reported by other authors. The scanning electron microscopy (SEM) method has shown the pattern of development of *C. albicans* yeast flora in the oral mucosa, which has been studied at sequential times during the development of acute oral candidiasis. At the onset of the disease, no fungal mycelium bundles have been found during SEM examination. By the third day of the disease, they are very few and small, which enables us to assess the state of local nonspecific resistance. By the seventh day after the onset of oral candidiasis, *C. albicans* filamentation is observed, as evidenced by the decrease in mycelial bundles. The results of these studies suggest that the appearance of signs of oral candidal infection is associated with epithelial desquamation and filamentation of *C. albicans*. The study of different types of vegetative cells of *C. albicans* will allow us to assess the stages of its cellular morphogenesis in order to prevent the development of COVID-associated oral candidiasis, to conduct earlier diagnostics and to plan treatment of patients with post-COVID-19 condition.

Keywords: mucous membrane of the oral cavity; resistance of the oral mucosa; post-COVID-19 condition; COVID-associated oral candidiasis; scanning electron microscopy.

Introduction

The coronavirus infectious disease COVID-19 has turned out to be an extraordinary global health crisis caused by the emergence of a post-viral syndrome – the long-term COVID condition, or post-COVID-19 condition (PCC). Based on the World Health Organization, the duration of COVID-19 symptoms after SARS-CoV-2 infection in those who have had the disease for two months and which cannot be explained by an alternative diagnosis is defined as PCC (Soriano et al., 2022). After SARS-CoV-2 infection, the incidence of PCC in the population is estimated to be 10%, and symptoms can occur immediately after recovery or recur over time (Ballering et al., 2022). Severe immunosuppression due to COVID-19 causes exacerbation of pre-existing infections and development of a number of new clinical signs. Recently, along with the increase in the number of patients with post-COVID-19 condition, the number of cases of invasive fungal infections has been growing among them (Akhtar et al., 2022).

The widespread use of corticosteroids, monoclonal antibodies/broad-spectrum antibiotics, and their cumulative dose increase the susceptibility of patients and can contribute to the development of candidiasis in previously immunocompetent individuals or to exacerbation of an existing fungal disease (Mehta & Pandey, 2020). In addition, long-term non-selective use of anabolic steroids causes immunosuppression and increased blood sugar levels, providing an environment for the rapid growth of microflora, including fungi, in various biotopes (Jawanda et al., 2021). The post-COVID-19 condition can cause multiple fungal superinfections in immunocompromised patients (Benhadid-Brahmi. et al., 2022). The three most common opportunistic fungal infections among patients with post-covid "tail" are mucormycosis, aspergillosis, and candidiasis (Jawanda et al., 2021). Candidiasis is the most common fungal infection, with *Candida* species present in 400,000 systemic fungal diseases (Mukaremera et al., 2017). *Candida* is known to be a dimorphic fungus that can exist in both yeast (blastospore, blastoconidial) and mycelial forms depending on the environment (Muzyka & Epifanio, 2013). The most common *Candida* species found both in healthy oral mucosa (OM), present in 30–55% of healthy adults, and in oral diseases, is *Candida albicans* (Millsop & Fazel, 2016). Oral signs and symptoms in the post-COVID-19 period are more likely to manifest as coinfections involving the oral mucosa in patients (Amorim et al., 2021). Oral symptoms due to SARS-CoV-2 infection, in addition to dysgeusia, ageusia, a sore and dry mouth, and severe halitosis, may include oral mucosal lesions that range from spots, nodules, plaques, depapillation of the dorsal surface of the tongue to pseudomembranes and multiple ulcers and vesiculobullous lesions (Mariz et al., 2020; Surboyo et al., 2021).

In oral mucosa diseases, due to the high level of pathogenicity of the fungus and the state of immunosuppression in patients, *C. albicans* is identified in more than 80% of cases (Vila et al., 2020). Invasive fungal infections in patients with immunosuppression associated with post-COVID-19 condition, due to their high prevalence, require the study of the pathogenesis of candidiasis and the patient's immune response to fungal aggression (Garcia-Vidal & Carratalà, 2012). The local immunity of the oral cavity as the first line of defense against infections caused, particularly, by various morphological forms of fungal flora, is known to affect the recognition of *C. albicans* wall components. Nowadays, more than 150 species of *Candida* are known to exist, of which the most common species involved in invasive infections are *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, and *C. krusei*, most of which grow only in the form of yeast (Garcia-Vidal & Carratalà, 2012).

An important factor in the virulence of the opportunistic human pathogen *C. albicans* is cellular morphogenesis, when the pathogen can transform into yeast, pseudohyphae or true hyphae. Such transformations result in the development of pathogenic forms that, with the support of region-specific conditions, penetrate human tissues, particularly the oral mucosa (Mukaremera et al., 2017). Conditions induced by *C. albicans*, when its yeast forms rapidly transform into a micellar, fungal form, are associated with a decrease in local resistance of the oral mucosa, which can cause surface desquamation of the mucosal epithelial layer, leading to erosive and ulcerative lesions. Moreover, *C. albicans*-induced oral mucosal diseases trigger recurrent irritants that may also have an immunological component, which helps explain resistance to antimicrobial drugs and reduced effectiveness of specific therapy (Song et al., 2018). Current observations demonstrate the importance of studying the pathogenesis of candidiasis, taking into account the morphology of *C. albicans*, changes in the composition of the pathogen cell wall that affect immune recognition (Mukaremera et al., 2017).

However, the relationship between the cellular morphogenesis of *C. albicans* and the immune recognition of this fungus remains unclear. Of all the species, *C. albicans* is the most common pathogen of mucosal and systemic infections, and it is responsible for about 70% of fungal infections worldwide (Mukaremera et al., 2017). For the last several decades, it has been the main cause of life-threatening invasive infections. The study of different types of vegetative cells of *C. albicans* will enable us to assess the stages of its cellular morphogenesis to prevent the development of COVID-associated oral candidiasis, to conduct earlier diagnostics and to plan treatment of patients with post-COVID-19 condition.

The aim of the study was to evaluate the sequence of morphological transformation of *C. albicans* during oral mucosa infection in patients with post-COVID-19 condition.

Materials and methods

Patients enrolled in the study were explained the purpose of the clinical trial and subsequently they signed an informed consent. The study was conducted at the City Dental Clinic of the Rivne City Council. The study complied with the bioethical standards of the Declaration of Helsinki of the World Medical Association "Ethical Principles for Medical Research Involving Human Subjects" (adopted by the 59th General Assembly, revised October 2008), the Declaration of Ethical Principles of the Ukrainian Helsinki Human Rights Union (2016), the International Code of Medical Ethics and the Laws of Ukraine (the decision of the Bioethics Commission of the Ivan Horbachevsky Ternopil National Medical University (minutes No. 75 of November 01, 2023).

The study involved 53 patients with acute candidal lesions of the oral mucosa with a previous history of COVID-19 and confirmed SARS-CoV-2 infection by sequencing or real-time PCR in respiratory samples. The identified manifestations of candidal lesions in the oral cavity in patients with post-COVID-19 condition were classified into three main categories: acute manifestations, chronic manifestations, and chronic syndromes of cutaneous and mucosal candidiasis (Singh et al., 2014; Millsop & Fazel, 2016; Hellstein & Marek, 2019). Out of the total number of examined patients with manifestations of COVID-associated candidiasis of the oral cavity, 21 patients were diagnosed with acute erythematous candidiasis, and 32 patients with relapse of acute pseudomembranous candidiasis.

During the observation period for the course of acute fungal stomatitis, cytological and morphological analysis of epithelial cells was performed to identify the stages of transformation of yeast forms of *C. albicans* into the fungal form. During the observation period, smear prints were taken from the mucous membrane of the affected area in all patients, then prepared on sterile slides and fixed with an alcohol-ether mixture for 5 minutes. The samples were dried using a gas burner and stained according to Romanowsky-Giemsa, followed by analysis according to the standard method (Weber & Huisken, 2012). After staining, the obtained cytological samples of smear prints were examined under an Olympus BX-41 microscope (Olympus Corporation, Tokyo, Japan, 2010) and the results were processed using the Olympus DP-soft (version 3.2; Soft Imaging System, Münster, Germany) for morphological examination with an assessment of the intensity of pathological reactions at different observation periods.

Simultaneously, scanning electron microscopy (SEM) was used to visualize and evaluate all aspects of the condition of the oral mucosa, the state of its colonization, and the phases of morphological evolution of *C. albicans* at different periods of observation (Howlett & Squier, 1980; Inoué, 1985; Kullaa-Mikkonen, 1987). Samples for SEM were prepared according to the generally accepted methodology and examined in a scanning electron microscope JEOL-25TA-220 (Japan Electron Optics Laboratory Co., LTD, Tokyo, Japan, 2006) immediately after preparation of smear prints, which allowed us to minimize artifacts caused by drying of the samples (Tian et al., 2008). The obtained SEM images for validation were analyzed at different microscope magnifications and processed using an image analyzer based on the UTHSCSA Image Tool® software (Developer: D. Wilcox, B. Dove, D. McDavid, D. Greer) (Schindelin et al., 2012).

Results

COVID-associated oral candidiasis is one of the most common manifestations on the oral mucosa. We focused on acute manifestations of COVID-associated oral candidiasis. During the examination of the oral cavity, the presence of various clinical forms in several areas of the oral cavity associated with *Candida* infection was observed simultaneously. Out of the total number of examined patients with manifestations of COVID-associated candidiasis of the oral cavity, 21 patients were diagnosed with acute erythematous candidiasis, of which 14 patients developed the pathology for the first time – *de novo*.

Since acute pseudomembranous candidiasis prevailed among the examined patients (60.38%), our attention was focused on this type of candidiasis. The high prevalence of pseudomembranous candidiasis – an opportunistic infection in immunocompromised patients after COVID-19, was apparently related to the immunosuppressive therapy the patients received. Apparently, the excessive growth of *Candida* was caused by oral dysbiosis after taking broad-spectrum antibiotics and corticosteroids for the treatment of patients with COVID-19. This form of candidiasis presented in various areas of the oral mucosa and manifested by multifocal yellow-white cheesy plaques, which were easily removed by careful scraping, revealing a hyperemic erosive surface. Painful erythematous lesions were observed throughout the oral cavity, in particular in the area of the back of the tongue with central atrophy of the papilla and in the area of the mucous membrane of the cheeks.

At the onset of acute oral pseudomembranous candidiasis, it was found that smear prints from the surface of the affected areas contained single lymphocytes and neutrophilic granulocytes with segmented and horseshoe-shaped nuclei in the center of the cell (Fig. 1).

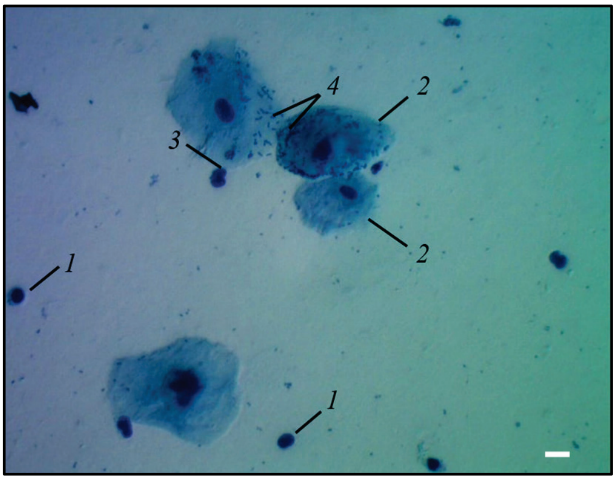

Fig. 1. Cellular composition of smear prints of the buccal mucosa at the onset of acute oral candidiasis: *1* – leukocyte; *2* – buccal epithelial cell; *3* – cytoplasmic contact between leukocyte and epitheliocyte; *4* – microorganisms; light microscopy, Romanowsky-Giemsa staining, scale bar = 5 μm

SEM examination of the sample of smear prints from the surface of the buccal mucosa of patients with acute candidal stomatitis revealed the cellular composition of the yeast-like form of *C. albicans* and *C. albicans* druses (Fig. 2).

During this period of observation of patients with oral candidiasis, a significant number of desquamated epithelial and immune cells, yeast forms of *C. albicans* were found in plaque33 on the affected areas of the oral mucosa, which transformed into a fungal form on the fifth day of the disease, which was confirmed by SEM examination and manifested by the formation of fungal hyphae (Fig. 3a). As seen in the SEM illustration, a typical fungal hypha penetrated the epithelial cell to form a localized defect in the epithelial layer of the oral mucosa.

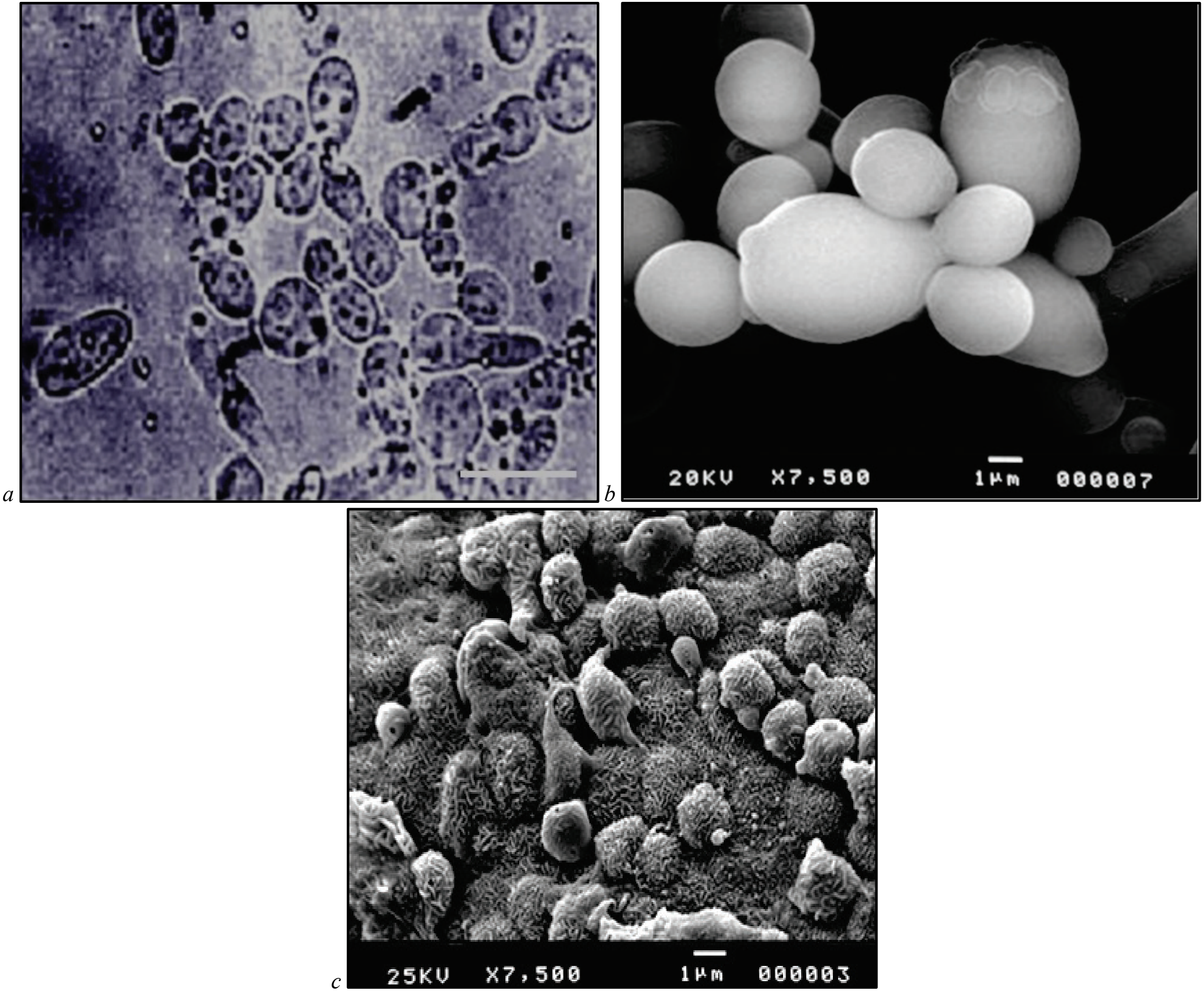

Fig. 2. Morphological illustrations of smear prints from the surface of the affected buccal mucosa of patients at the onset of oral candidiasis: *a* – cellular composition of the yeast-like form of *C. albicans* (light microscopy, Romanowsky-Giemsa staining, Scale bar = 5 μm); *b*, *c* – scanning electron microscopy: structure of the yeast-like form of *C. albicans* (*b* – accelerating voltage 20 kV; *c* – accelerating voltage 25 kV; scale bar = 1 μm)

A decrease in local nonspecific resistance of the oral mucosa and the general immunity of patients might be confirmed by the appearance of growth buds on *C. albicans* yeast cells, apart from the beginning of transformation of yeast forms into fungal forms (Fig. 3b). The figure showed elongated blastoconidia with several scars located at the cell poles and the initial stage of *C. albicans* transformation into a fungal form, the appearance of growth buds and scars on the surface of the blastospore during the induction of the fungal hypha.

This revealed typical fungal hyphae that penetrated epithelial cells, which proved the activity of *C. albicans* cell evolution in acute candidiasis. The general view of the surface of the buccal epithelium during fungidization with *C. albicans* is shown in Figure 4. In those areas where hyphae developed, intercellular contact was impaired, the edges of epithelial cells curled and diverged, a local defect was formed, as a result of which the epithelial layer lost its integrity and mechanical stability and no longer played a barrier role in the local nonspecific immunity of the oral cavity.

After 10 days from the onset of the disease, SEM examination revealed both single, short and long filaments of fungal hyphae (Fig. 5). As the figure showed, the detail of the short hyphae revealed its “umbilical” distal end, which penetrated the epitheliocyte. Long micellar filaments were freely located on the surface of epithelial cells, and they were always located in loci where there were defects of the oral mucosa of various sizes. In many areas of the oral mucosa, fungal hyphae were arranged in the form of bundles of long micellar filaments, and in some epithelial cells, rounded holes remained in the plasmalemma of epithelial cells in the area of micellar filament penetration as the site of the previous location of the fungal hyphae (Fig. 6). As demonstrated by the SEM illustration, a thick bundle of hyphae was closely connected with numerous desquamated epithelial cells of the oral mucosa.

After 15 days from the onset of the acute course of the disease, fungal mycelial hyphae of various lengths penetrated epithelial cells so quickly that defects in the oral mucosa did not have time to form (Fig. 7) and the surface cells were in close contact with each other.

At this stage of oral candidiasis, a large number of desquamated epithelial cells with well-defined fungal hyphae bundles in the area with epithelial desquamation could be recognized on the affected surface of the oral mucosa (Fig. 8). Morphological examination of the oral mucosa 15 days after the onset of oral candidiasis revealed a typical pattern with significant desquamation of the flattened surface epithelium with polygonal cells, which represented a complex labyrinth of coarse randomly arranged microfolds on the surface (Fig. 9a) in contrast to the microrelief of the epithelium in the normal state (Fig. 9b). Only a few loci were detected in which yeast forms of *C. albicans* were present on the epithelial surface.

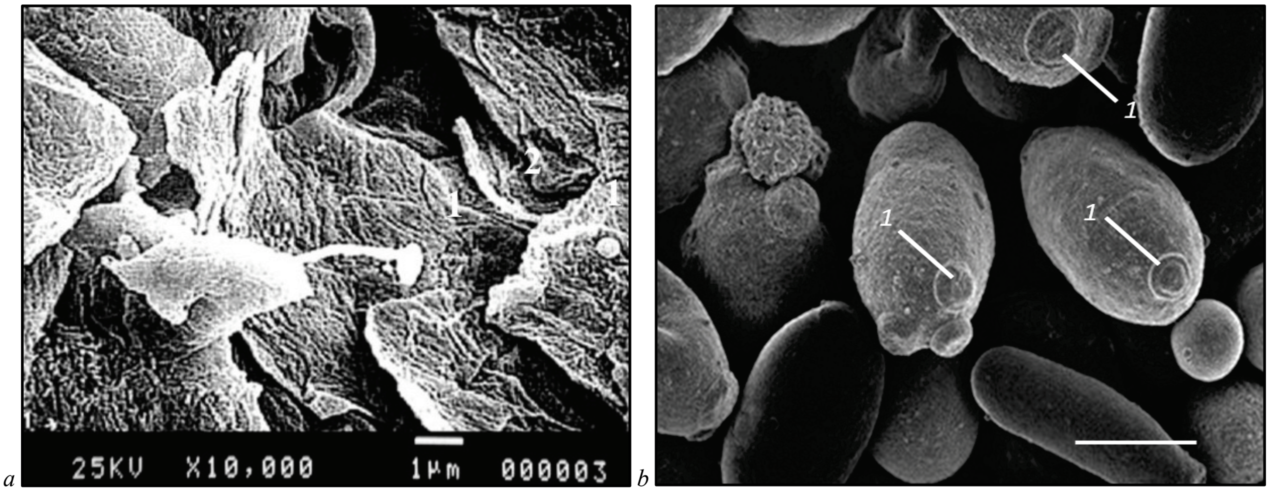

Fig. 3. Scanning electron microscopy: *a* – general view of the oral mucosa epithelium on the fifth day of oral candidiasis: morphological structure of the fungal form of *C. albicans*, typical hypha (*1*), local defect in the epithelial layer of the oral mucosa (*2*); accelerating voltage 25 kV; scale bar = 1 µm; *b* – elongated blastoconidia with scars on the cell poles, the appearance of growth buds and scars on the surface of the blastospore (1); scale bar = 2 µm

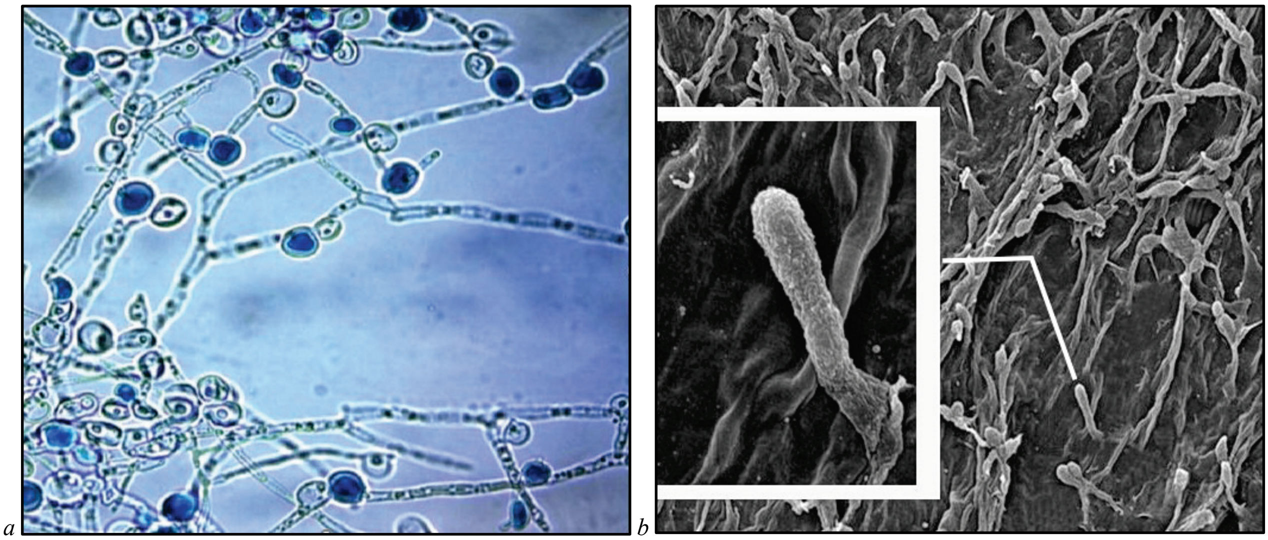

Fig. 4. General view of the buccal epithelium surface during *C. albicans* fungidization on the fifth day of the disease: *a* – light microscopy, Romanowsky-Giemsa staining, scale bar = 50 µm; *b* – scanning electron microscopy, accelerating voltage 20 kV; scale bar = 5 µm; footnote: a single hypha that grows on the epithelial surface; scale bar = 1 µm

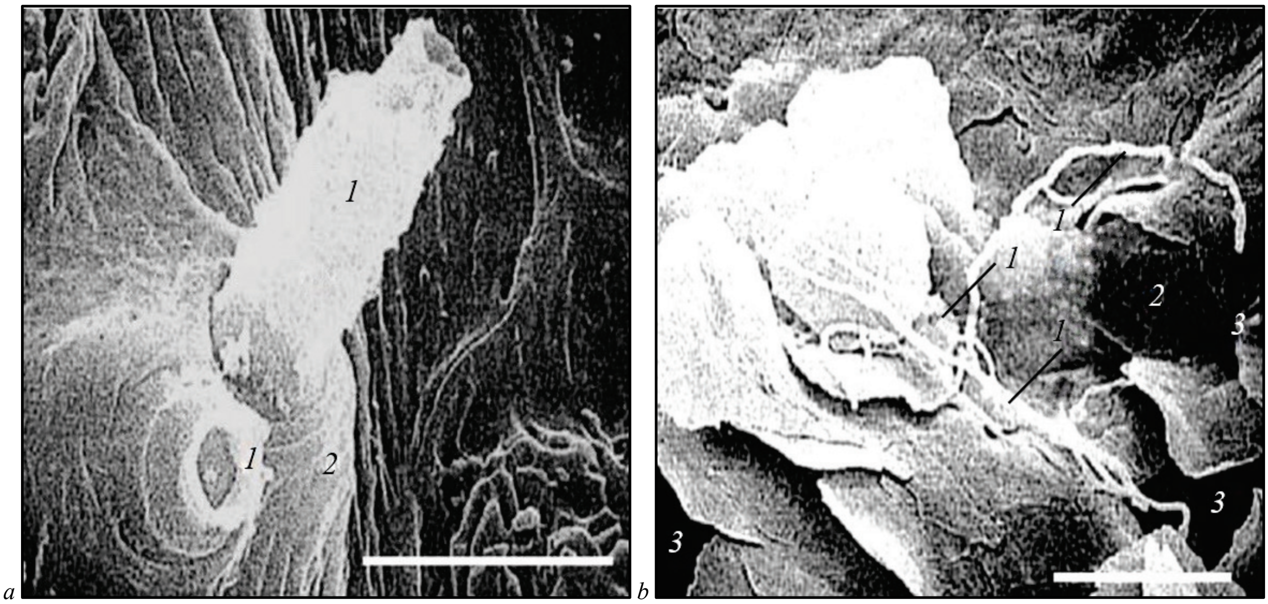

Fig. 5. Method: scanning electron microscopy: *a* – a fragment of the affected area of the oral mucosa on the tenth day of the disease: short filaments of fungal hyphae (*1*), epitheliocyte (*2*); scale bar = 100 µm; *b* – general view of long micellar filaments (*1*) located on the surface of epithelial cells (*2*) in loci with defects of the oral mucosa (*3*); scale bar = 50 µm

Therefore, the study and understanding of the molecular mechanism underlying the morphological phases of *C. albicans*, in particular, the development of fungal hyphae, one of the best-studied factors of its virulence, will enable us to expand the understanding of the etiopathogenesis of COVID-associated oral candidiasis in patients and identifying potential targets of *C. albicans* and its new mechanisms for choosing treatment strategies.

Discussion

It is currently known that reported cases of oral manifestations of COVID-19 might represent a new etiopathogenic mechanism between ACE2 and SARS-CoV-2. A number of studies reported that the combination of SARS-CoV-2's impact on the body's immunity, immunodeficiency states, and the treatment regimen for patients with COVID-19 affected the immune system, creating optimal conditions for various pathogenic fungal infections. As reported by Jawanda et al. (2021), severe secondary infections could occur during COVID-19 or even after the recovery phase, including fungal infections, which were often the leading cause of death. For example, the researchers mentioned that mucormycosis, a rare fungal infection caused by *Mucor*, *Rhizopus*, *Lichtheimia*, *Cunninghamella*, which were non-pathogenic for immunocompetent individuals, could be fatal for those with immunodeficiency. In patients with compromised immunity, mucoromycetes fungi infection occured, the main way of infection being inhalation of their spores, their germination in the nasal cavity and, due to the spread in the peripheral nervous system, invasion of the palate, orbits and brain, which caused death (Mehta & Pandey, 2020). The *Mucor* fungus showed an extraordinary affinity for blood vessels, forming blood clots in the arteries, which led to a decrease in blood supply and the development of tissue necrosis (Jagtap et al., 2021). There were reports of a patient with type 2 diabetes with aggressive mucormycosis as a consequence of Covid-19, illustrating the possible consequences of Covid-19 for the patient's body and the need for early diagnosis (Pathak et al., 2021). In patients with diabetes mellitus treated with SARS-CoV-2 using corticosteroids, there was a significant increase in the incidence of angioinvasive maxillofacial fungal infections (Moorthy et al., 2021). Blood infections caused by *Candida auris*, a multidrug-resistant fungus that can cause invasive infections, were detected in patients with COVID-19 (Prestel et al., 2021).

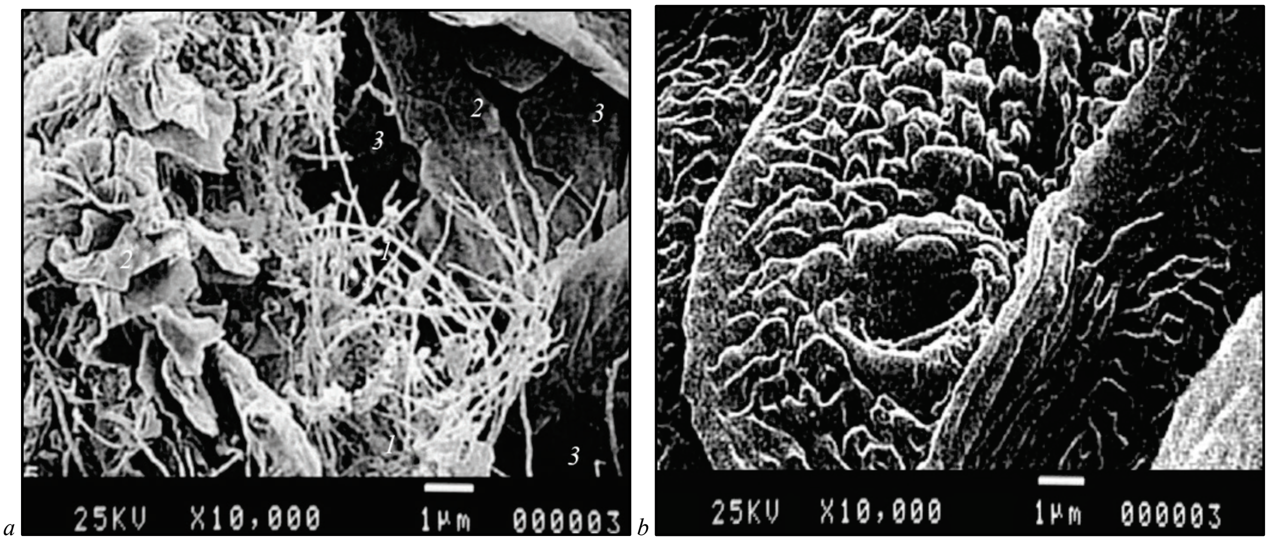

Fig. 6. Scanning electron microscopy: *a* – general view of the oral mucosa on the tenth day of the disease: *1* – a thick bundle of hyphae; *2* – desquamated epithelial cells; *3* – defect of the epithelial layer, scale bar = 100 µm; *b* – general view of an epithelial cell: *1* – round hole in the plasma membrane of the epithelial cell, scale bar = 50 µm, accelerating voltage 25 kV

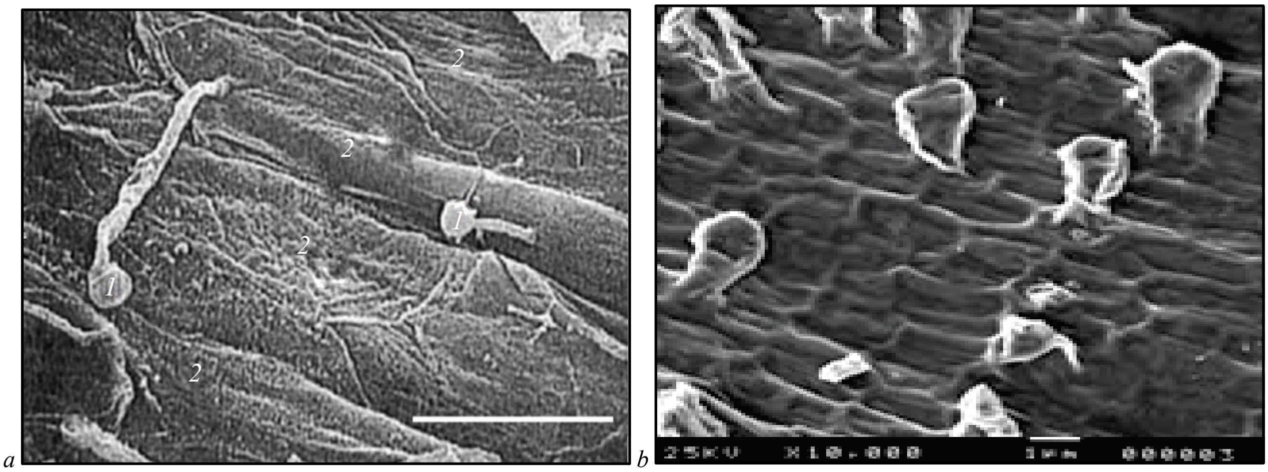

Fig. 7. Scanning electron microscopy: general view of the surface of epithelial cells of the oral mucosa 15 days after the onset of the disease: *a*: *1* – fungal mycelial hyphae; *2* – epitheliocyte, scale bar = 100 µm; *b*: accelerating voltage 25 kV, scale bar = 1 µm

Candidiasis appeared to be the most common fungal infection of the oral cavity diagnosed in people with immune system dysfunction or as a result of local or systemic drug treatment (Muzyka & Epifanio, 2013). The most common oral fungal infection caused by *Candida* species was *C. albicans*. It should be noted that *Candida* is an obligate microorganism found in the human digestive tract, in particular in the oropharyngeal region in 60% of healthy people without immunodeficiency (Gangneux et al., 2020). As a manifestation of the immunodeficiency state, chronic and recurrent candidal infection was observed in patients with COVID-19, which could subsequently progress to candidiasis of other parts of the gastrointestinal tract (Hellstein & Marek, 2019). The fungus *C. albicans* is often a benign representative of the mucosal flora, but it caused diseases of the oral mucosa in vulnerable patients with immunodeficiency, causing life-threatening infections.

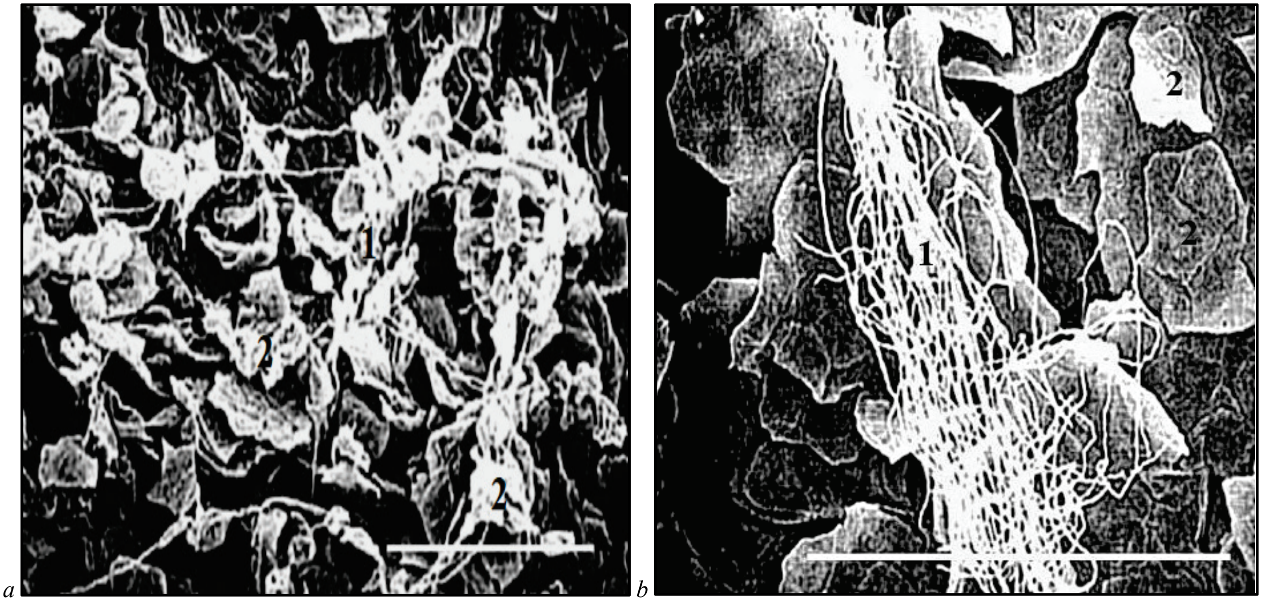

Fig. 8. Scanning electron microscopy: *a* – general view of the oral mucosa after 15 days of oral candidiasis: *1* – fungal hyphae bundle; *2* – desquamated epithelium, scale bar = 1000 μm; *b* – a well-defined mycelium bundle in the area with epithelial desquamation, scale bar = 100 μm

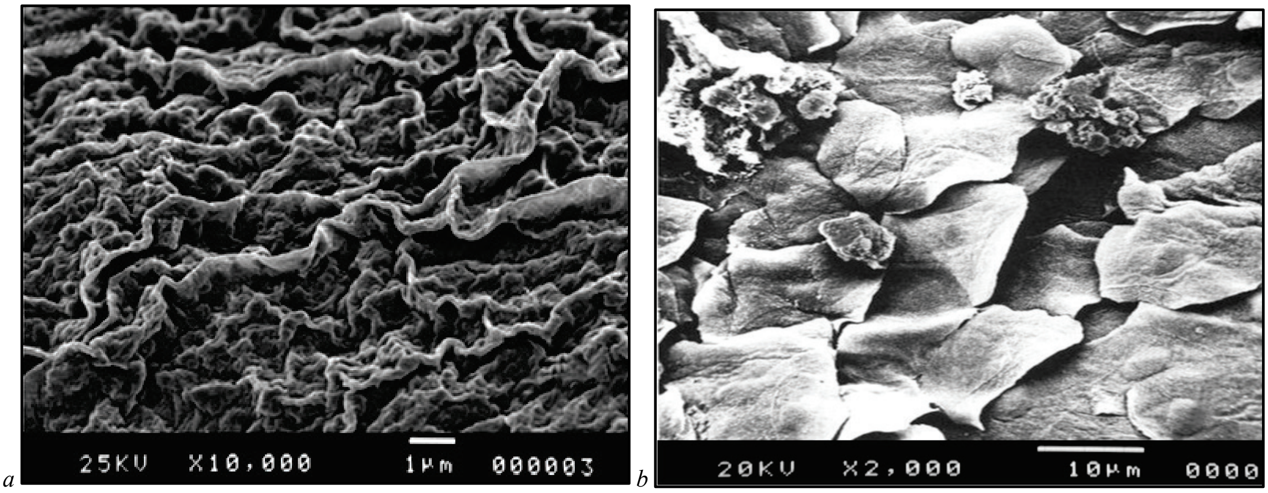

Fig. 9. General view of the surface of the oral mucosal epithelium: scanning electron microscopy: *a* – desquamated epithelium 15 days after the onset of oral candidiasis; accelerating voltage 25 kV; scale bar =1 μm; *b* – normal epithelial microrelief; accelerating voltage 20 kV; scale bar =10 μm

Fungal infections of the oral cavity and maxillofacial area could occur in high-risk patients with weakened immune systems. The most common manifestations of fungal infections in the oral cavity involved both primary lesions of the oral cavity and the result of a disseminated disease such as invasive candidiasis (Telles et al., 2017). Recently , it has been found that in cases of immunodeficiency, HIV-infected patients experienced increased levels of Candida, which colonized the oral mucosa, leading to its lesions (Vidya et al., 2016). Moreover, in some HIV-positive people, *C. albicans* tended to be more virulent, due to the state of severe immunosuppression, which ultimately determined clinical outcomes. In addition, the relationship and underlying mechanisms that might be involved in malignant transformation by *Candida* fungi and the development of oral squamous cell carcinoma were investigated (Mohd Bakri et al.). A distinctive feature of *C. albicans* biology included its ability to grow in yeast, pseudohyphal and hyphal forms, which represented an important phase in the disease process, and could cause tissue damage by penetrating the epithelial cells of the mucous membrane, primarily of the oral cavity, causing damage to the oral mucosa.

We first reported the transformation of *C. albicans* from a yeast-like to a fungal form in chronic recurrent aphthous stomatitis in patients with COVID-associated oral candidiasis. However, the very possibility of such an *in vitro* transformation was reported by other authors (Bauer & Wendland, 2007; Barnett, 2008). The important thing to consider was the fact that this transformation was combined with a change in the clinical course of candidiasis, accompanied by fever, regional lymphadenitis, dyspraxia, etc. The mentioned clinical manifestations arouse an increased interest in finding the underlying causes and factors of such an exacerbation of the clinical picture, and the desire to compare morphological changes with clinical manifestations of oral candidiasis. In our opinion, the study (Lehle & Tanner, 1976), which studied the effect of tunicamycin on the development and transformation of *C. albicans* in the laboratory, was also interesting, but the researchers' work stopped at this stage because the drug itself had increased toxicity and was not allowed to enter the clinical stage.

Our study showed that the first filaments became evident at the onset of the disease, with the detection of only yeast forms of *C. albicans*. There was a very close relationship between epithelial cells even at the time of filamentation, and often fungi with a new hypha were found to be completely covered by plasmalemal strips of the infected cell. In addition, when examined during the period of the disease, the shape of some hyphae was represented by a typical "bundle" variant of hyphal penetration. The results of our study revealed a significant effect of *C. albicans* fungidization on the morphological features of oral candidiasis in patients with post-COVID-19 condition. Determining the mechanisms of oral candidiasis as a pathological process caused by the excessive growth of *Candida* versus *Candida* as a commensal microorganism (from the Latin cum – "together with" and mensa – "table") could contribute to early diagnosis. Understanding of *C. albicans* morphological transformation, pathogenesis and host immune response to its transformation could help to optimize the treatment of fungal infections in patients with post-COVID-19 condition using appropriate antifungal agents. Knowing these processes would help dentists develop antifungal and immunomodulatory therapies and adequate preventive measures.

Summarizing the results of recent studies in various fields of fungal cell biology, which played an important role in understanding hyphal growth, mycelial formation, including morphological studies of *C. albicans* phases, their regulatory growth mechanism, and virulence factors, provided a theoretical basis for identifying targets for the treatment of candidiasis (Sudbery, 2011; Chen et al., 2020). Considering the above, for the early diagnosis of oral candidiasis, it is recommended to screen patients with COVID-19 systematically for fungal pathogens and invasive fungal diseases in in order to optimize rapid specific antifungal treatment (Gangneux et al., 2020).

Conclusions

Colonization of the oral mucosa with yeast forms of *C. albicans* as a commensal microorganism is a constant phenomenon and is not associated with clinical severity or other features of the course of diseases of the oral mucosa. Transformation of yeast forms of *C. albicans* into fungal form is associated with clinical exacerbation and other features of oral candidiasis, which requires the use of fungicidal drugs. Fungal forms of *C. albicans* cause desquamation of the oral mucosa epithelium with the formation of epithelial lining defects, which, in the presence of secondary microflora, cause the formation of erosive lesions. Monitoring the condition of the oral mucosa, depending on the state of local nonspecific resistance and the degree of colonization of the oral mucosa with yeast forms of *C. albicans*, should be included in the standard algorithm for examination of oral candidiasis in patients with a history of COVID-19.

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The authors declare no conflict of interest.

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