DOI https://doi.org/10.30525/978-9934-26-549-5-7

SOME ASPECTS IN PATHOGENESIS CANDIDASIS OF THE ORAL CAVITY

ДЕЯКІ АСПЕКТИ В ПАТОГЕНЕЗІ КАНДИДОЗУ РОТОВОЇ ПОРОЖНИНИ

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Over the last years, there have been changes in the evolution, prognosis, diagnosis, and treatment of fungal diseases [1]. The relevance of the problem of mycotic stomatitis is caused by the increase in the number of patients suffering from acute and chronic recurrent diseases, as well as by the increase in resistance to antifungal drugs [2, 3]. Given the great medical and social importance of the problem of fungal lesions, intensive research into the basic mechanisms of its pathogenesis is being conducted [4, 5]. However, despite this, the candidiasis pathogenesis remains poorly understood [6].

There are four forms of C. albicans: yeast, hyphae, pseudomycelium and spores. The ability of yeast to turn into hyphae is considered one of the most important pathogenic features of C. albicans. The transition of C. albicans from a harmless commensal to an opportunistic pathogen occurs in parallel with its morphological transformation from a fungus to a hyphal form [7]. The virulent properties of Candida spp. include their ability to form a biofilm with microbes encapsulated in a self-secreted extracellular matrix. This formation is a conglomerate of biomolecules and hydrolytic enzymes, in particular lipases, proteinases, and phospholipases.

The increased resistance of fungi is associated with their ability to interact and secrete low-molecular hormone-like molecules. This mechanism is known as *quorum sensing* (QS), and the molecules responsible for intermicrobial interaction are designated as QS molecules. Currently, four main QS molecules are described *in the fungal kingdom*: farnesol, thyrosol, phenethyl alcohol, and tryptophol. These QS molecules of *Candida* fungi contribute to the regulation of various key functions, such as pathogenesis, morphogenesis, and filamentation. Among QS molecules, farnesol and

thyrosol are known to be involved in biofilm formation modulating several virulence factors of the fungus, including its dimorphic transition. In particular, farnesol induces the transition of hyphae to yeast and inhibits biofilm formation, while thyrosol has the opposite effect stimulating hyphal production and, accordingly, playing a key role in the formation of biofilms [8, 9].

In addition to biofilms, adhesin proteins and persistent cells further increase their resistance contributing to the candidiasis recurrence [10]. Characteristic features of Candida are the capacity for fixation on the mucosa, its colonization and penetration.

It has been established that gastrointestinal dysbiosis leads to metabolic immunosuppression affecting local and systemic immunity, and indicates the relationship between dental condition and immunological status [11]. Against the background of immunodeficiency states, the process generalization with dissemination and the appearance of secondary foci in various tissues and organs is possible [12].

The immune mycotic stomatitis response represents a regulatory system of opposing pro- and anti-inflammatory mediators from different cellular sources to balance immune homeostasis, which, in turn, differentiates commensal and pathogenic forms of Candida and includes natural immune mechanisms for the prevention of fungal infections in healthy people. The production of anti-inflammatory cytokines (IL-17) and chemokines plays an important role in the epithelial immune response against Candida infection, leads to the involvement of neutrophils, key cells of the anti-candida mycotic stomatitis immunity [13]. The interaction of C. albicans with macrophages is an important protective response of the immune system to candidiasis associated with the deep spread of Candida cells in the human body [14]. C. albicans causes a protective allergic reaction through platelet Th2 and Th17 polarization. Platelets contribute to the respiratory tract protection from mycosis of C. albicans via an antifungal pathway involving candidalysin, GPlbα and Dkk-I providing Th2 and Th17 responses [15]. It has been established that C. albicans colonization stimulates a wide range of human body responses being the major target of antifungal antibodies, including blood serum IgG and intestinal IgA, as well as circulating antifungal Th17 cells [16]. An imbalance in interaction between hematopoietic and nonhematopoietic cells leads to the proliferation of commensal fungi and provokes the disease progression.

A key element in innate immunity playing an important role in suppressing C. albicans infection by activating the pectin complement pathway is mannan-binding lectin. The level of mannan-binding lectin is markedly increased during infectious lesion of patients with invasive candidiasis, which indicates its role at an early disease stage. Mannans of the cell wall of C. albicans mask ß-(1,3)-glucan from recognition by pectin-1 contributing

to evasion of innate immunity. IgE is often detected to mannan and protein agents of fungi. Since increased IgE production reflects the T2 lymphocyte activity degree suppressing antifungal cellular immunity, the detection of an intensive increase in IgE concentration can serve as a prognostic indicator of an unfavorable infectious process course. Suppression of the Th1 lymphocyte activity contributes to the phagocytosis weakening, since there is no reinforcement (reactivation) of macrophages and neutrophils by the immune system [17, 18]. The cell wall of C. albicans is a structure consisting of polysaccharides and proteins, and is divided into inner and outer layers. It is not a static structure, but is constantly rebuilt in response to environmental influences. The outer layer is mainly composed of mannose and proteins, mainly O- and N-type mannose polymers (mannose) covalently linked to proteins forming glycoproteins. Among them, O-chain mannan, N-chain mannan, and phosphorylated mannan are major pro-inflammatory factors providing key functional properties such as cell adhesion required for virulence. The inner layer is composed of skeletal polysaccharides, ß-1,3-glucan, ß-1,6-dextran and chitin, and its main components give shape and advantages for cell survival. ß-1,3-glucan is a relatively minor component, but is considered a critical matrix polysaccharide because it is associated with biofilm resistance to antifungal drugs and hinders drug diffusion [19, 20].

Therefore. Further in-depth study of the main mechanisms, upon which the increase and decrease in the pathogenic potential of fungi depends, including the growth of hyphae susceptible to the influence of environmental stimuli, the antagonistic bacterial flora, the immunologic protection influence during the candidal lesion course, is promising in order to develop fundamentally new approaches to the treatment and prevention of this patient population.

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DOI https://doi.org/10.30525/978-9934-26-549-5-8

STRUCTURAL AND FUNCTIONAL CHANGES OF THE LIVER IN PATIENTS WITH HYPOTHYROIDISM

СТРУКТУРНО-ФУНКЦІОНАЛЬНІ ЗМІНИ ПЕЧІНКИ У ХВОРИХ НА ГІПОТИРЕОЗ

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Вступ. Гіпотиреоз є одним із найбільш поширених ендокринних розладів, що впливає на функціональний стан багатьох органів і систем, зокрема печінки. Щитовидна залоза та печінка тісно пов'язані між собою через метаболічні та гормональні механізми: вісь щитовидної залози має глибокий вплив на енергетичний метаболізм у печінці, включаючи печінковий ліпогенез та окислення жирних кислот. Печінка не тільки отримує сигнали від гормонів щитовидної