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The Role of Candida Infection in Pathological Processes in the Body

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Abstract: Candidiasis is a mycotic infection caused by yeast-like fungi of the genus Candida. The genus Candida belongs to the domain (superkingdom Supraregnum) Eukaryota, the kingdom (Regnum) Fungi, the division (Phylum) Ascomycota, the subdivision (Sub-Phylum) Ascomycotina, the class (Classis) Saccharomycetes, the subclass (Subclassis) Ascomycetidae, the order (Ordo) Saccharomycetales, the family (Family) Saccharomycetaceae, and the genus (Genus) Candida.

Keywords: candida, infection, pathological, pneumonia, atypical pneumonia.

In recent years, the number of fungal infections has significantly increased, with candidiasis being of the greatest practical importance. The development of candidiasis is facilitated by numerous factors, which are classified as direct and indirect, exogenous and endogenous. J. McNeil and V. Kan identify the following groups of factors: - Physiological conditions; - Local aggravating factors; Diseases associated with metabolic disorders and endocrinopathies; - Neoplasms, infectious diseases, exhaustion; - Immune deficiency; - Medicinal factors; - Surgical interventions.

Due to the growing number of factors leading to diseases caused by fungi of the genus Candida spp., there has been increasing interest among researchers worldwide in organ and tissue damage caused by these opportunistic microorganisms.

This genus includes non-sporulating yeasts, where pseudomycelium can be well-developed, rudimentary, or entirely absent, with some species forming true mycelium. The genus Candida spp. consists of 163 species, but only a limited number of them play a significant role in human pathology, with C. albicans being overwhelmingly dominant. Yeast fungi of the genus Candida are widely distributed in nature and are considered unique microorganisms demonstrating a wide range of adaptive capabilities. In various ecological niches of the human body, these fungi can exist both as stable commensals and as successful opportunists.

Previously, the primary causative agents of candidiasis were mainly recognized as five species: C. albicans, C. guilliermondii, C. krusei, C. pseudotropicalis (now known as C. kefyr), and C. tropicalis. However, currently, 19-20 species of Candida (anamorphs) are frequently reported as causative agents, including: C. africana, C. albicans, C. albicans var. stellatoidea, C. catenulate, C. ciferrii, C. dubliniensis, C. famata var. famata, C. famata var. flareri, C. glabrata, C. guilliermondii, C. kefyr, C. krusei, C. lipolytica, C. lusitaniae, C. norvegensis, C. parapsilosis, C. pelliculosa, C. tropicalis, C. viswanathii, C. zeylanoides.

The frequency of isolation of these species varies depending on the region and epidemiological circumstances. Generally, Candida species are cosmopolitan.

Like any disease, candidiasis is characterized by various stages with typical damage to internal organs and systems. Colonization combined with tissue reactions (hyperemia, edema, infiltration) is considered the first stage of the candidiasis process.

The second stage of the candidiasis process involves the penetration of fungal elements into surface tissues, leading to the development of a superficial invasive process. The first and second stages of candidiasis may persist for months or even years. The third stage—penetration of surface tissues and fungal invasion into lymphatic and blood vessels, with subsequent involvement of deep tissues and organs—is referred to as deep organ tissue candidiasis. The fourth stage, fungemia, and the formation of candidiasis foci distant from the initial site of infection correspond to systemic and generalized forms of candidiasis.

Understanding the fundamentals of candidiasis pathogenesis is essential for laboratory specialists to provide accurate diagnostic conclusions.

Fungal cultivation requires knowledge of their biological characteristics. The yeast phase of Candida spp. consists of relatively large unicellular organisms, measuring 1.5 × 1.5 to 8 × 14 µm, with oval, round, or elongated shapes. These organisms grow relatively quickly on solid and liquid nutrient media, especially those supplemented with carbohydrates. The optimal growth temperature is 25–28°C; species pathogenic to humans and animals grow well at 37°C. Their thermal range is 5–40°C, with an optimal pH of 5.8–6.5, though they can grow in acidic environments with a pH as low as 2.5–3.0.

These fungi are facultative anaerobes, with anaerobic metabolism particularly characteristic of the filamentous phase. The cell wall predominantly contains carbohydrates (92%), of which mannose accounts for 86%, glucose 6%, and 96% of the carbohydrates are glycosidically linked to proteins. Minor components include D-galactose, D-xylose, and phosphate, while proteins constitute only 7%. The cell wall also contains chitin, with higher concentrations found in the mycelial phase.

The incubation period for culturing these fungi ranges from 7 to 10 days, depending on the type of clinical material being analyzed. The lengthy cultivation process presents significant challenges for practitioners. Current unresolved issues include the widespread implementation of improved nutrient media for isolating different fungal species. The delayed issuance of results often leads to clinicians losing interest in the final conclusions provided by mycologists.

It is no secret that the success of mycological research relies on synthesizing theoretical knowledge of the clinical progression of various opportunistic diseases. Candidiasis is an opportunistic mycosis characterized by diverse localization (skin, mucous membranes, lungs, gastrointestinal organs, etc.). Opportunistic fungi of the genus Candida spp. are a normal component of the human digestive tract microbiota, where they exist as saprophytes.

In recent years, a clear trend has emerged regarding the transition of Candida species from a saprophytic to a parasitic state in the host's body . This transition is facilitated by certain pathogenic factors of the fungi, such as their adhesive properties, as well as impaired immune resistance in the host. Intensive multiplication of Candida spp. in the oral cavity can lead to lesions of the mucosal lining. In the distal esophagus of patients with gastroesophageal reflux disease, microbial imbalances have been documented, often dominated by microorganisms producing various pathogenic enzymes, including C. albicans with properties like germ tube formation and increased adhesion to epithelial cells.

In fecal samples, Candida species are isolated in up to 80% of cases, while on intact skin, their prevalence is approximately 9.5%. The overall carriage rate is established by the age of 16–18 years and remains relatively stable thereafter. Among Candida spp., Candida albicans accounts for 50–80% of isolates from the mucous membranes of the gastrointestinal and urogenital tracts. C. albicans is responsible for approximately 90% of local candidiasis cases and 50–70% of generalized cases.

Inadequate etiological therapy can artificially select clinically significant strains that exhibit resistance to various drugs. Changes in the quantitative balance of the microbiota in any biosubstrate can lead to dysbiotic shifts. According to Avalueva E.B. and colleagues (2009), all patients (100%) receiving prednisone treatment exhibited candidal dysbiosis of the large intestine upon microbiological stool analysis, with Candida spp. levels averaging 6.89 lg CFU/g (reference values: no more than 3 lg CFU/g). All patients showed reduced lactobacilli counts and increased levels of opportunistic microbiota (mainly Enterobacter spp. strains in combinations of two or three species). Candida albicans was found in 20% of cases, C. tropicalis in 47%, and C. krusei in 33%.

Infections of the gastrointestinal tract caused by Candida spp. are, unfortunately, common. Clinically, fungal overgrowth in the intestine may present as asymptomatic carriage, invasive mycotic processes (specific dysbiosis), or invasive candidiasis, with these conditions sometimes representing sequential stages in the progression of candidiasis. It is well-known that adhesion always precedes colonization. The ability of Candida spp. to adhere to the mucosal surfaces of the host strongly correlates with their pathogenicity. Candida spp. often employ indirect adhesion mechanisms, such as co-adhesion to bacteria.

Therefore, studying the biological characteristics of clinical copro-isolates of Candida spp. is crucial to developing a database on the phenotypic variability of Candida spp. in specific regions.

Of particular note is the increasing prevalence of mycotic lesions of ENT organs in recent decades. The detection and treatment of fungal infections in otolaryngology have gained greater relevance due to their widespread nature, predisposing factors, and more severe clinical courses. However, the role of fungi in inflammatory diseases of the upper respiratory tract (URT) is often underestimated, leading to misinterpretation of the disease etiology and inappropriate treatment.

In a study by Baiduisenova A.U. and colleagues (Astana, 2009), comprehensive examinations of patients with chronic pharyngitis and tonsillitis revealed mycotic lesions in 42 cases. Among these, Candida albicans was identified in 20 patients, C. tropicalis in 5, C. krusei in 2, C. kefyr in 3, Cryptococcus spp. in 4, and rare cases of C. guilliermondii, C. parapsilosis, and C. norvegica.

These findings emphasize the need for regular microbiological monitoring of fungal infections in the respiratory system, including ENT organs. Such data would strengthen interdisciplinary collaboration and aid in developing improved diagnostic algorithms.

In this regard, Khusnarizanova R.F. and colleagues (Russia, 2009) studied the prevalence of yeast-like and mold fungi in patients with occupational chronic bronchitis. The authors analyzed the medical histories and microbiological sputum tests of 239 hospitalized patients aged across a wide range. A diverse microbial landscape was identified, with most yeast-like fungal strains (62.35%) comprising C. albicans, followed by C. tropicalis (14.12%), C. glabrata (9.41%), C. parapsilosis (7.06%), C. krusei (3.35%), and others (3.35%).

The dominance of C. albicans highlights its significant role in mycotic infections.

Currently, the prioritization of studying tuberculosis morbidity in the Republic of Kazakhstan remains pressing. It is well known that the presence of Candida species in tuberculosis patients stimulates the growth and reproduction of Mycobacterium tuberculosis, accelerates the formation of pulmonary cavities, and influences the development of various clinical complications of the disease.

Kazakhstani researcher M.Z. Sarsenbayeva (2006) examined 899 tuberculosis patients hospitalized at the National Center of Phthisiatry (NCP) in Kazakhstan. Among these, 352 patients (23.1%) had Candida species isolated. Candida was identified in oral mucosal smears in 36.4% of cases, in feces in 25.7%, in sputum in 21.7%, and in bronchoalveolar lavage in 2.0%. The author demonstrated that candidiasis more frequently developed in patients with extensive

destructive and chronic forms of tuberculosis, such as caseous pneumonia (41.7%), fibrous-cavernous tuberculosis (35.3%), and disseminated tuberculosis (33.3%).

The frequency of nosocomial fungal infections is increasing, and the issue of antifungal resistance is becoming more acute. Many new antifungal drugs are being introduced into clinical practice, which may increase the role of fungi as etiopathogens of emerging complications. Consequently, resistance to antifungal agents is an inevitable concern in such cases. Vrychan N.A. and colleagues (St. Petersburg, 2009) studied the species distribution and susceptibility of Candida spp. strains isolated from the blood of hospitalized patients in St. Petersburg between 2003 and 2008. They found that in 75.2% of cases, the causative agents of candidemia were non-C. albicans micromycetes.

The role of fungal infections in gynecology among women of reproductive age is also growing. Candida spp. are among the most common opportunistic micromycetes encountered in obstetrics and gynecology. Urogenital candidiasis is 2-3 times more common in pregnant women than in non-pregnant women.

It is also essential to address the issue of Candida carriage. Four main types of Candida carriage are distinguished:

1. Transient carriage: Lasting several days, with a single detection of fungi in low amounts.

2. Short-term carriage: Lasting 3-4 weeks.

3. Prolonged carriage: Lasting up to three months.

4. Chronic carriage: May last for years, typically with high levels of fungal colonization.

Research from the All-Union Mycological Center underscores the importance of differentiating candidiasis from Candida carriage. Colonization of epithelial tissues without signs of inflammation may be considered carriage. Even in the absence of clinical manifestations, Candida carriage can have subtle effects on an otherwise healthy individual. Thus, widespread investigation of carriage rates among at-risk groups is promising for physicians across specialties to prevent mycotic damage to various organs and systems.

An analysis of the literature shows that Candida spp. occupies a leading position in the microbial landscape of sputum, blood, oral mucosa, posterior pharyngeal wall secretions, feces, and vaginal discharge. Large-scale studies in Kazakhstan are clearly warranted. Covering diverse nosological forms (organs and systems) will facilitate the creation of a unified database that systematically documents the biological properties of clinical Candida spp. strains, including their resistance to many contemporary antifungal drugs. This is crucial for selecting effective etiological therapies.

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