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Candida: A Common Fungi Affecting Human Health

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Abstract

Background*: The incidence of fungal infections and candidiasis in particular has increased significantly in last few decades. Candida species are one of the important cause of nosocomial infections.*

Aetio-pathogenesis*: Increased use of broad spectrum antibiotics, intravenous catheters, cancer chemotherapy and an increased number of immunocompromised patients have resulted in the increase of candida infections. Factors like Germ Tube formation, adhesion to the host cell, phenotypic switching, production of enzymes along with formation of biofilm are important for determining its pathogenicity. Knowledge of the virulence factors is important for understanding its pathogenesis.*

Clinical spectrum*: In most individuals, it is a harmless commensal. However it is capable of causing infections that ranges from superficial mucocutaneous infections to life threatening disseminated infections like candidemia. Its capacity to cause infections depends on imbalance between its virulence factors and certain defects of the immune system. There are three major forms of disease: oropharyngeal candidiasis, vulvovaginal candidiasis, and invasive candidiasis.*

Prevention*: This fungal infection can be prevented by keeping a healthy life style including good hygiene and proper nutritional intake along with rational use of anti-biotics.*

Keywords*: Candida, nosocomial infection, germ tube, biofilm*

1. INTRODUCTION

Candidiasis is one of the most common fungal disease affecting mucosa, skin, nails and internal organs. It is caused by various species of fungus belonging to the genus Candida with candida albicans as the representative species. Over the last few decades, Candida species has emerged as an important cause of nosocomial infections [1]. Increased use of broad spectrum antibiotics, intravenous catheters, neutropenia, cancer chemotherapy and an increased number of immunocompromised patients have resulted in the increase of candida infections [1]. Around 20 pathogenic species are known including C.albicans, C. tropicalis, C. krusei, C. glabrata, C. parasilopsis, C. kefyr, C. dubliniensis. C. albicans is still the most common pathogenic virulent species isolated but other species can also be pathogenic.

Although C.albicans is the most common species causing infections but shift towards non-albicans Candida species is evident in recent years [2]. Among non albicans species, C. tropicalis is most commonly isolated from various clinical samples [3]. C. tropicalis has the ability to develop rapid resistance to fluconazole. Therefore its increasing isolation is of great concern. Virulence factors like germ tube formation, adhesion to the host cell, phenotypic switching, production of enzymes along with formation of biofilm are important for its pathogenicity.

2. MORPHOLOGY

There are 3 morphological forms- budding yeast, pseudohyphae, hyphae.

C. albicans appear as oval budding yeast like cell, gram positive with formation of pseudohyphae. For its pathogenicity, its ovoid-shaped budding yeast and true hyphal forms are the most important.

3. VIRULENCE FACTORS

This is the most common opportunistic pathogen, utilizing several kinds of virulence factors. Factors like germ tube formation, adhesion to the host cell, phenotypic switching, production of enzymes along with formation of biofilm are important for its pathogenicity. Knowledge of these virulence factors is important for understanding its pathogenesis. Expression of these virulence factors depends on various factors like the species causing infection, geographical origin, type of infection, the site and stage of infection and host reaction.

Adhesins

Its ability to adhere to host cell is related to their virulence and plays major role in its pathogenesis. Well-known adhesins are agglutinin-like sequences (ALS) that are members of a family of seven glycosylated proteins. They have special sets of

glycosylphosphatidylinositol (GPI)-linked cell surface glycoproteins that allow it to adhere to the receptors of host cell.

Biofilm formation

Another important virulence factor of Candida albicans is the ability to form biofilms on living and non-living surfaces, such as mucosal membranes and catheters, respectively. Rather it has the ability to form biofilm on most medical devices [4].

Biofilm formation by fungi may play an important role in pathogenesis. Biofilms are the organized structures involving microbial communities that are attached to some inanimate surfaces or tissues and circumvented in a matrix of exopolymeric materials. Biofilm formation is initiated by irreversible adherence of microbial cells to tissues or devices and followed by growth and maturation to form a mesh of cells with altered phenotype, growth rate, and gene expression compared to planktonic cells. Formation of Biofilms is a sequential process including adherence of yeast cells to the substrate, proliferation of these yeast cells, formation of hyphal cells in the upper part of the biofilm, accumulation of extracellular matrix material and finally, dispersion of yeast cells from the biofilm complex [5].

Increased resistance may be due to the complex architecture of biofilms, the biofilm matrix, increased expression of drug efflux pumps and metabolic plasticity [6]. There are evidences suggesting that the majority of disease produced by C. albicans is associated with formation of biofilm. Biofilms may help maintain the role of fungi as pathogenic by evading host immune mechanisms, resisting antifungal treatment and withstanding competitive pressure from other organisms. Consequently, biofilm-related infections are difficult to treat. Biofilm production is also associated with a high level of antimicrobial resistance of the associated organisms.

Hsp90, a major heat shock protein is involved dispersion of biofilms. Its ability to form biofilms on catheters, endotracheal tubes, pacemakers and other prosthetic devices has contributed to its predominant prevalence in nosocomial infections [7,8]. Detection of biofilm is important as it leads to development of resistant nosocomial infections.

Hydrolytic enzymes:

Secretion of hydrolytic enzymes is an important determinant for its pathogenicity. They facilitate active penetration into the host cell. Proteases, phospholipases and lipases are the 3 important hydrolases expressed by Candida albicans.

Secretion of proteinases is important to degrade the tissue barriers and obtain nutrition at the infection site. About 10 secreted aspartic proteases (Sap1-10) are known. SAP1–6 genes is related to adherence, tissue damage and changes in the immune response. Secreted aspartyl proteinases (SAPs) hydrolyze many proteins such as albumin, hemoglobin, keratin, collagen, laminin, fibronectin, mucin, salivary lactoferin, interleukin1b, cystatin A and Immunoglobulin A. It is reported that production of SAPs is also correlated with hyphal formation, adherence, and phenotypic switching [9,10].

Phospholipases are enzymes that hydrolyze ester linkages of glycophospholipids and hence impart tissue invasiveness to Candida cells. 4 major classes (A, B, C, and D) of phospholipases are found and all 5 members of the B class are involved with the disruption of a host cell surface. Phospholipase concentrated at the hyphal tip may be related to invasiveness of this form. There is an increased level of phospholipase production in species isolated from blood compared to commensal isolates.

There are around 10 members of lipases namely LIP1-10. Lipases causes digestion of lipids for nutrient acquisition, adhesion to host cells and tissues, unspecific initiation of inflammatory processes by affecting immune cells and self-defence by lysing the competing microflora.

Toxins

Glycoprotein extracts of its cell wall (endotoxins) are also involved in determining its pathogenicity.

Complement receptors

Ability to bind to complement derived opsonins might influence its virulence.

Phenotyping switching

C. albicans is a polymorphic fungus and its ability to switch between different morphological forms is considered siginificant for its pathogenicity. It can grow either as ovoid-shaped budding yeast, as elongated ellipsoid cells with constrictions at the septa (pseudohyphae) or as parallel-walled true hyphae [11]. Further, hyphal cells have stronger adherence capacity due to expression of ALS adhesins and also exhibit greater invasiveness to tissues than the yeast form.

4. PATHOGENICITY

This fungus produces various manifestations depending on the immune status of the host and underlying predisposing factors. An infection caused by Candida is termed candidiasis or candidosis. Clinical disease ranges from superficial mucocutaneous infections to life threatening disseminated infections like candidemia. There are three major forms of the disease caused by candida: oropharyngeal candidiasis, vulvovaginal candidiasis, and invasive candidiasis.

In oropharyngeal candidiasis, infection occurs in the mouth or throat. It occurs in infants, individuals with diabetes mellitus, patients on antibiotics, patients with HIV. White plaque is present on oral mucous membranes known as oral thrush. Infection may remain confined to buccal mucosa, gums, tongue or may become diffuse. C. albicans is the main cause of oral candidiasis in patients with HIV infection.

Vulvovaginal candidiasis causes rash, itching, burning and curdy discharge from the genital region [12]. Affects young and middle aged females particularly during their active reproductive life. Vulvovaginitis is mainly due to C. albicans. However, other species of Candida such as glabrata, parapsilosis, and tropicalis are emerging [12].

Invasive candidiasis occurs when it enters into the bloodstream and from blood it can easily spread to other organs of the body. It includes urinary tract candidiasis, candiduria, endocarditis, pericarditis, pulmonary candidiasis, meningitis, osteomyelitis, endophthalmitis, candidemia and septicemia.

5. DIAGNOSIS

Prompt an early diagnosis should be done because these infections have high mortality. Diagnosis is very difficult because of the absence of specific signs and symptoms.

a. Direct examination of clinical samples should be done by KOH mount, gram staining. Yeast cells are 4-8 um with budding and pseudohyphae.
b. Fungal culture: specimens should be cultured on Sabouraud dextrose agar with added antibiotics at 25° C and 37° C. Colonies appear in 3-4 days as cream colored, smooth and pasty.
c. Germ tube test: germ tube are seen as long tube like projections from the yeast cell without any constriction at the point of attachment. This test is used for presumptive identification of Candida species.
d. Chlamydospore formation: seen on corn meal agar after incubation at 25° C. There is formation of large, thick walled highly refractile terminal chlamydospores after 2-3 days of incubation.
e. Biochemical tests: sugar fermentation and assimilation
f. CHROMagar candida: rapid plate based test for simultaneous isolation and identification.different species are identified based on their color.
g. Immunodiagnosis: ELISA, Radio immunoassay. Counter current immunoelectrophoresis ,Slide agglutination.

6. TREATMENT

Gentian violet (1%) nystatin and azoles can be used locally. For systemic infections azoles, amphotericin B, flucytosine can be used. Antifungal susceptibility testing should be done as drug resistance is increasing now a days.

7. PREVENTION

This fungal infection can be prevented by keeping a healthy life style including good hygiene and proper nutritional intake.

8. CONCLUSION

The incidence of fungal infections is increasing significantly and so its morbidity and mortality. This is caused by an increase in antimicrobial resistance and the restricted number of antifungal drugs. Candida species are major human fungal pathogens that cause both mucosal and deep tissue infections. The increased incidence of systemic mycoses caused by Candida species in hospitalized patients is an important cause of morbidity and mortality worldwide, especially in critically ill patients. Knowledge of the pathogenicity mechanisms of C. albicans, their virulence factors, and their interaction with host defense mechanisms is important for the development of new antifungal therapies and diagnostics. Despite the effectiveness of available antifungals in combating such infections, the emergence of drug resistance to antifungals, and problems of toxicity and poor delivery of drugs at the target site in systemic infections, have necessitated a systematic approach to the study of fungal pathogens, host–fungi interactions, and identification of virulence factors. Formation of drug resistant biofilms is an important factor in their contribution to human disease. Biofilms play an important role in the perpetuation of these infections primarily with respect to their ability to adhere to various medical devices. There is a need to search for new products with effective antifungal abilities due to the adverse side effects of existing medications, increasing emergence of strains that are resistant to conventional antifungal agents, and the formation of biofilms in medical devices and tissues.

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