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Commensal and pathogen: Candida albicans

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Abstract

Candida albicans is ubiquitous, dimorphic yeast which resides in oral cavity as commensal. But it also acts as pathogen under certain specific circumstances and causing most common infection of oral cavity called oral thrush. An extensive review is made to discuss various forms of candida infection, predisposing factors and management of candidal infection.

Keywords: Candidiasis, Steroids, Denture stomatitis, Angular cheilitis.

Introduction

Oral candidiasis is the most common opportunistic infection seen in immunocompromised patients caused by candida albicans which is commensal of oral cavity. Host immune system determines whether it remains as a commensal in oral cavity or transforms into a pathogen. Severity of candida infection is variable, ranging from non life threatening superficial mucocutaneous lesions to invasive disseminated infection involving multiple body organs.(1) It was found that Candida albicans isisolated from the oral cavity of 45% neonates, 45%–65% of healthy children, 30%–45% of healthy adults,50%–65% of people who wear removable dentures, 65%–88% of people those are under acute and long term care facilities, 90% of patients with acute leukaemia undergoing chemotherapy, and 95% of HIV patients.(2-8) Candida albicans causes 4th most common nosocomial infection with mortality rate of 39% in year 1995 and it is 3rd most common nosocomial infection in ICUs with mortality rate of 47%.(9)

Classification

According to clinical appearance, oral candidiasisis classified into three types: pseudomembranous, erythematous (atrophic) and hyperplastic.

Pseudomembranous: It is the most common type, also called thrush. It is frequently seen in neonates, immunocompromised patients and those taking topical corticosteroid therapy. The characteristic feature of this type is coating or individual patches of Pseudomembranous white slough and on scraping, it leaves erythematous and sometimes minimally bleeding mucosa. These pseudomembrane areas are described as curdled milk or cottage cheese. It can be present in any area of oral cavity but usually seen on tongue, palate and buccal mucosae.(10)

Erythematous: It is relatively rare and occurs in both acute and chronic forms. It was also known as antibiotic sore mouth due to its association with long term use of antibiotics. The chronic form is usually seen in HIV patients, present on dorsum of tongue, palate and very less seen on buccal mucosa. Lesions are painful, localized erythematous areas. It is only painful form of candidiasis.(1,11) Lesions on dorsum of tongue result in loss of papilla. Differential diagnosis includes denture stomatitis, erythema migrans, erythroplakia and anemia.(12)

Hyperplasic: It is also known as candidal leukoplakia. Clinically it presents as white plaque that cannot be wiped away. It usually involves commissural region of buccal mucosa, frequently on both sides of mouth.(10,13) It occurs in two variants that are homogeneous adherent white plaque or erythematous multiple nodular/ speckled type.(14,15) This type has positive association with smoking and may have varying degrees of dysplasia. It can also occur in association with iron and folate deficiencies and with defective cell mediated immunity.(1)

Other forms of candidiasis

Denture stomatitis: It is chronic inflammation of mucosa mainly restricted to denture area, so also known as chronic atrophic candidiasis. It is seen in 50-65% of patients wearing dentures. Clinically lesions of denture stomatitis are pinpoint hyperaemia, diffuse erythematous or granular/papillary type. Usually it remains asymptomatic but occasionally patient may complain of burning sensation and soreness. There are some causative factors for denture stomatitis like poor oral hygiene, nocturnal denture wear, ill fitting prostheses and restricted salivary flow.(11,16,17)

Median rhomboid glossitis: It is chronic symmetrical area on tongue anterior to circumvallate papillae due to atrophy of filiform papillae. Biopsy of this area found candida in 85% of cases.(18) Clinically surface of lesion is smooth or lobulated.(19) Usually it remains asymptomatic but some patients complain of persistent pain, irritation or pruritus. It is commonly associated with smoking and inhalation of steroids.(17,20,21)

Angular cheilitis: It is characterized by erythematous fissuring at one or both corners of mouth and

commonly caused by candidal infection. It may be caused by staphylococci, streptococci and chronically moist area created by facial wrinkles at corners of mouth and along nasolabial fold in older people, vitamin B12 deficiency and iron deficiency anemia.[11,22,23]

Linear gingival erythema: it is linear band of erythematous gingivitis. It typically occurs in HIV patients, therefore termed as HIV gingivitis. Its lesions may present with bleeding. C. dubliniensis has also been found as pathogen for it in addition to candida albicans.[17]

Predisposing factors for oral candidiasis: These are divided into local and systemic factors.

Local factors

Impaired saliva secretion: Malfunctioning of salivary glands can lead to oral candidiasis. Saliva contains antimicrobial proteins such as lactoferrin, sialoperoxidase, lysozyme and specific anticandida antibodies that interact with oral mucosa and prevent overgrowth of candida. Therefore diminished salivary secretion can increase risk of oral candidiasis.[24,25]

Drugs: Inhaled or topical steroids and excessive use of antimicrobial mouthwashes suppress local cellular immunity and phagocytosis, therefore increasing risk of candidiasis. Immunity becomes normal on discontinuation of these drugs. Use of broad spectrum antibiotics impair normal ecological balance of oral micro flora and eliminate competing bacteria, resulting in increased development of oral candidiasis.[10,26,27]

Dental prostheses: Dental prostheses such as dentures make a favorable anaerobic microenvironment for candida growth, with low oxygen and low pH. This may be due to increased adherence of candida to acrylic of prostheses, improperly fitted dentures, reduced saliva flow under dentures and inadequate oral hygiene.[27,28]

Smoking: Smoking increases risk of oral candidiasis by various mechanisms such as localized alteration in epithelium, smoking along with denture friction changes mucosal surface, suppression of local immunity, elevation of glycosylated hemoglobin and smoking also increases adrenaline levels, thus indirectly affecting blood glucose level.[1,29,30]

Systemic factors

Age: Extremes of age may also increase risk of oral candidiasis due to reduced immunity.[31]

Nutritional status: Deficiency of iron reduces fungistatic action of transferrin and other iron dependent enzymes. Other nutrients which are deficient in candidiasis are vitamin A, B6, magnesium, selenium, zinc, folic acid and essential fatty acids.[32,33]

Endocrine disorders: Studies reported that prevalence of oral and invasive candidiasis is more in patients with diabetes and Cushing's syndrome.[34,35]

Immune disorders: Conditions of immune deficiency such as AIDS and severe combined immunodeficiency syndrome, increase risk of candidiasis.[36]

Treatment

The aim of any oral thrush treatment is to prevent rapid spread of fungus, but the best approach may depend on age of patient, overall health of patient and cause of fungal infection. Treatment should include recognition of underlying cause, history of medications, immunological and endocrine disorders, nutritional deficiency and prolonged hospitalization.

Antifungal agents are: polyenes (nystatin and amphotericin B), ergosterol biosynthesis inhibitors-the azoles (miconazole, clotrimazole, ketoconazole, itraconazole, and fluconazole), allylaminesthiocarbamates, and morpholines and DNA analog 5-fluorocytosine, and newer agents such as caspofungins.[37,38]

In healthy patients superficial oral candidiasis is generally treated topically while immunocompromised patients are treated systemically as well as topically. Patients with persisting predisposing factors and relapsing candidiasis should be treated with antifungal agents with lowest risk of development of resistant strains.[39,40] The commonly used first line antifungal agents for treatment of oropharyngeal candidiasis(OPC)are: fluconazole, clotrimazole, nystatin. On the other hand second line agents are: itraconazole, posaconazole, voriconazole and agents used in refractory OPC are: caspofungin, micafungin, anidulafungin, amphotericin B.[41]

The use of topical or systemic antifungal agents for treating of OPC has resulted in the development of resistant Candida species.[42] The biofilm organization of fungus enables it to survive in unfavorable conditions and resulting in high resistance of fungus to antifungal medications.[43] Because of increased resistance of this pathogen to conventional treatment, new treatment strategies have been searched.

Antimicrobial Photodynamic Therapy (APDT) is common anticancer treatment used for inactivation of microorganisms.[44,45,46] This therapy makes use of photosensitizing agent (PS)and light corresponding to absorption band of PS.[45] The interaction of these two in the presence of oxygen, produces reactive oxygen species(ROS) which causes oxidative damage and death of microorganisms.[47]

Predominately used PS drugs are phenothiazinium dyes[44,45] porphyrins[48] 5-aminolevulinic acid[49] and phenothiazines.[50]

Photodithazine (PDZ) is a second-generation photosensitizer and it is a glucosamine salt of chlorin derivative soluble in water.[51] This PS produces shorter periods of photosensitization, longer activation wavelengths and higher yields of singlet oxygen than first-generation PS.[52]A study conducted on immunosupressed mice concluded that APDT is safe

and effective to treat oral candidiasis as it has antimicrobial activity without any damage to host tissues.[53]

Conclusion

Candida albicans is part of normal oral micro flora. But when it becomes pathogen, it causes damage to host tissues as it has ability to adhere to host surfaces, produce filamentous growth and release hydrolytic enzymes. Therefore care should be taken so as to prevent conversion of this commensal microorganism into pathogen. Also Candida develops resistance to some conventional antifungal agents, so constant research is needed for effective and safe strategies to treat oral candidiasis.

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