Mucosal Candidiasis

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Updated: Feb 12, 2016

Background

Candidosis (candidiasis, moniliasis) describes a group of yeastlike fungal infections involving the skin and/or mucous membranes, including the mouth. Infection is caused by *Candida* species, typically, *Candida albicans*.[1]

C albicans is ubiquitous and is found mainly on oral or genital mucosae; it may also be transmissible between consorts.[2] Candida is an opportunistic infection and typically occurs where the local ecology is disturbed, or where there is an immune defect.

Candidosis is seen orally in people with altered oral ecology (from dental appliances, hyposalivation, or the local use of immunosuppressants or antimicrobials) and/or impaired immunity (eg, transplant recipients, persons on immunosuppressive treatments, persons with HIV/AIDS or oral cancer, various cellular immune defects).[3, 4, 5]

By tradition, the most commonly used classification of oral candidosis divides the infection into 4 types including (1) acute pseudomembranous candidosis (thrush), (2) acute atrophic (erythematous) candidosis, (3) chronic hyperplastic candidosis, and (4) chronic atrophic (erythematous) candidosis.

Chronic hyperplastic candidosis was further subdivided into 4 groups based on localization patterns and endocrine involvement including (1) chronic oral candidosis (candidal leukoplakia), (2) endocrine candidosis syndrome, (3) chronic localized mucocutaneous candidosis, and (4) chronic diffuse candidosis.

Thrush (acute pseudomembranous candidosis) is the term used for the multiple white-fleck appearance of acute candid0sis, which purportedly resembles the appearance of the bird with the same name.

Erythematous candidosis is the term used for the red lesions of candidosis.

Pathophysiology

C albicans is a commensal organism inhabiting the mouths of almost 50% of the population (carriers); persister cells are clinically relevant, and antimicrobial therapy selects for high-persister strains in vivo.[6] T cells and interleukin (IL)–17 are protective.[7] *C albicans* prevacuolar protein sorting gene VPS4 is required for extracellular secretion of the secreted aspartyl proteases Sap2p and Saps4-6p. Furthermore, the vps4Δ null mutant has been shown to be markedly hypovirulent in a murine model.[8] These authors found VPS4 contributes to several key aspects of oral epithelial but not uroepithelial infection, and in contrast to systemic infection, plays no major role in the pathogenesis of candidal vaginitis. Although a defect in the chemokine receptor CX3CR1 increases susceptibility of mice and humans to systemic candidiasis, it does not in mucosal candidosis.[9] Cx3cr1 is dispensable for the induction of IL-17A, IL-22, and IL-23 in the tongue after infection, as well as for the clearance of mucosal candidiasis from the tongue or lower gastrointestinal (GI) tract colonization. Furthermore, the dysfunctional human CX3CR1 allele CX3CR1-M280 was not associated with the development of recurrent vulvovaginal candidiasis (RVVC) in women.

C albicans is the predominant causal organism of most candidosis. Other species, including *Candida krusei*, have appeared in persons who are severely immunocompromised. *Candida glabrata* is an emerging cause of oropharyngeal candidosis in patients receiving radiation around the head and neck.[10] In patients with HIV infection, new species, such as *Candida dubliniensis* and *Candida inconspicua*, have been recognized.

Animal models for oral candidosis are available.[11]

Acute pseudomembranous candidosis (thrush)

Thrush may be observed in apparently healthy neonates (who have not yet developed immunity) or in persons in whom antibiotics, corticosteroids, or hyposalivation disturb the oral microflora. In premature neonates, systemic candidosis may arise.[12]

Oropharyngeal thrush occasionally complicates the use of corticosteroid inhalers or other topical preparations. Immune defects, especially HIV infection,

immunosuppressive treatment, leukemias, lymphomas, cancer, and diabetes, may predispose patients to candidal infection.

Erythematous candidosis

Erythematous candidosis may cause a sore red mouth, especially of the tongue, in patients taking broad-spectrum antimicrobials. It also may be a feature of HIV disease. Median rhomboid glossitis is a red patch occurring in the middle of the dorsum in the posterior area of the anterior two thirds of the tongue and especially is observed in smokers and in those with HIV disease.

Chronic hyperplastic candidosis

Chronic hyperplastic candidosis typically presents as a leukoplakia often at the angles of the mouth or on the tongue, and it has a higher malignant potential than some other leukoplakias. This is especially the case when associated with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy.[13]

Chronic mucocutaneous candidosis

Chronic mucocutaneous candidosis (CMC) describes a group of rare syndromes, which sometimes include an immune defect that has been identified, and in which persistent mucocutaneous candidosis responds poorly to topical treatment. Generally, the more severe the candidosis, the greater the likelihood that immunologic defects (particularly of cell-mediated immunity) can be identified. Recent studies suggest a defect in cytokine (IL-2 and interferon-gamma) production in response to candidal and some bacterial antigens, with reduced TH1 lymphocyte function and enhanced TH2 activity (and increased IL-6), and reduced serum levels of immunoglobulins G2 and G4.

Epidemiology

Frequency

United States

Candidosis is common in groups at risk, such as patients who are immunocompromised. Frequency of infection is rising, primarily because of HIV infection and both the increase in candidal species other than *C albicans* and the resistance to antifungals.

International

Candidosis is common in groups at risk, such as patients who are immunocompromised.

Sex

Candidosis is reported equally in males and females worldwide, except in areas where males with HIV infection outnumber females.

Age

Candidosis predominantly occurs in middle-aged or older persons; however, in those with HIV infection, candidal infection primarily occurs in the third and fourth decades.

Clinical Presentation

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Disclosure: Nothing to disclose.

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Disclosure: Nothing to disclose.

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Disclosure: Nothing to disclose.

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Disclosure: Nothing to disclose.

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