Case Report

Oral Candidiasis in Patients with Level CD4+ Below 50

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Abstract

Approximately 90% of individuals diagnosed with HIV/AIDS have encountered Oral Candidiasis during the progression of their disease, especially in patients with a reduced CD4+ 200 mm³. Oral Candidiasis is a prevalent opportunistic infection of the oral cavity. Reported a case of a patient with oral candidiasis in an HIV/AIDS with CD4+ below 50 and discussed the mechanism of molecular relationship decreasing count CD4+ with virulence of Candida Albicans.

In this report, we present a case of a 35-year-old female who presented with oral candidiasis. The patient's CD4+ count test revealed a level below 50 and HIV test I-II-III reactive. Human immunodeficiency Virus causes a decrease in CD4+ count and leads to opportunistic oral candidiasis infection.

Keywords: oral candidiasis; HIV; AIDS; CD4+

INTRODUCTION

Oral candidiasis is an opportunistic infection primarily impacting the oral mucosa.1 The predominant causative agent of these lesions is Candida albicans (C. albicans), a pathogenic organism derived from the normal commensal flora.2 Candidiasis primarily impacts individuals who are in the vulnerable stages of life, including the very young, the elderly, and those who are immunocompromised due to severe illness.1 Oral candidiasis, a prevalent form of mucocutaneous candidiasis, is frequently observed in individuals infected with Human Immunodeficiency Virus (HIV)/ Acquired Immune Deficiency Syndrome (AIDS) on a global scale.3 Approximately 90% of people who have HIV/AIDS have encountered oral candidiasis throughout their illness.3 Patients with oral candidiasis have elevated viral load and decreased levels of CD4+ T lymphocytes.4 Oral Candidiasis, a condition characterized by the presence of Candida species, is mostly attributed to C. albicans, according to prior research.4 However, recent studies have indicated a rise in the incidence of oral candidiasis caused by Candida non-albicans strains.4

This paper reports a case of Oral Candidiasis in an HIV-infected patient with a CD4+ count below 50. It discusses the molecular mechanism of C albicans transformation from a commensal organism to an AIDS-related pathogen.

CASE REPORT

A 35-35-year-old female patient came to the emergency room with complaints of coughing, breathlessness, and debris for three days. The general condition was comatose (GCS 425), the temperature 39 °C, and oxygen saturation (SpO2) 61. A thorax examination photo revealed a process of parahilary and
paracardial pneumonia in Sinistra. Sars-Cov 2 PCR resulted in negative. Anti-HIV reagents I, II, and III results were reactive, and the CD4+ count was below 50 because the CD4+ count is so low that the exact amount cannot be detected.

Intra-oral examination in the first visit showed that a thick pseudo membrane, whitish color, in the lower and upper labial mucosa, palate durum and molle, and tongue can be scrapped and left erythema base and felt pain (Figure 1). The pseudo membrane was scrapped and subjected to microbial culture and direct examination. No other lesion was found in the oral cavity.

The oral lesion was then debridement using normal saline, followed by 0.2% chlorhexidine digluconate 0.2%, and oral nystatin 100,000 IU/ml was applied to the entire mouth and lip lesion was applied with borax glycerin.

At the next visit, an intra-oral examination still found pseudomembranes on the palate, and the gingiva thinned (Figure 2). The patient's complaints of pain and thickness were reduced. Debridement using normal saline, followed by chlorhexidine di gluconate 0.2%, and oral nystatin 100,000 IU/ml to the entire mouth was continued, and fluconazole injection 2 mg/ml was added. The internist gave ARV therapy consisting of Tenovir 300 mg, Lamivudin 300 mg, and Efavirenz 600 mg.

The blood analysis showed a decrease in hemoglobin, hematocrit, and lymphocytes. Anti-toxoplasma IgG was reactive (537.5 IU/ml). The direct microbial examination of the swab results tongue using Vitex® 2 Compact showed Candida Albicans colonies automatically. By microscopic examination, the KOH staining showed a hifa of Candida (Figure 3).

The diagnosis in this patient was oropharyngeal candidiasis associated with HIV/AIDS due to CD4+. In this patient, clinically in his oral cavity, white pseudomembrane could be scraped in almost the entire oral cavity, mostly in the palate area to the oropharynx. The patient felt the surface of his oral cavity was rough, thick, and sore.

Informed consent was obtained prior to the preparation of the case report, and the authors endeavored all efforts to ensure anonymity.

Figure 1. The oral mucosa in the patient with pseudomembranous dorsum of the tongue (A) and palate (B)
Figure 2. The oral mucosa in the patient with pseudomembranous of gingiva (C) and palate (D)

Figure 3. The direct examination of the microbial and pseudomembranous samples showed a candida colony with KOH staining. The observation used microscopic light with 400 magnifications.
**DISCUSSION**

The CD4⁺ cell count provides an indicator for evaluating the development of a disease.⁵ When the count of CD4⁺ cells falls below 200 cells/mm³, individuals become susceptible to several pathogenic mechanisms related to AIDS, leading to an increase in developing secondary infections.⁶ In our case, the count of CD4⁺ cells falling below 50 cells/mm³ (< 5%) signifies the progression to the AIDS very advanced stage. Based on clinical and supporting examination, oropharyngeal candidiasis has occurred. Based on the study, this secondary infection starts to occur at CD4⁺ counts 200/mm³.³

HIV has a prolonged influence by targeting the immune system, resulting in its compromised state and impaired functionality.⁵,⁷ HIV infection results in decreased levels of CD4⁺ cells through various methods, including apoptosis of uninfected bystander cells.⁸ The phenomenon of direct elimination of infected cells through viral death and the eradication of infected CD4⁺ T cells by CD8⁺ cytotoxic lymphocytes that can recognize infected cells is observed.⁶ When the CD4⁺ T cell count decreases below a certain threshold, the functionality of cell-mediated immunity is impaired, leading to an increased susceptibility to opportunistic infections.⁵

CD4⁺ cells are responsible for stimulating the release of interleukin-17 (IL-17) in mucosal tissues.⁹ IL-17 is involved in the maintenance of the structural barrier of the GI tracts and mucosal immunity and is driven by the production of IL-22.⁹ The mucosal immune response against C. albicans is facilitated by the mechanistic actions of IL-17 and IL-22.⁹ These cytokines act on epithelial cells expressing IL-17R, leading to the production of potent Antimicrobial peptides (AMPs) such as β-Defensin,
S100A8/A9, and Histatins, which play a crucial role in protecting against invasive infection and inhibitory effects on the colonization of C. albicans on epithelial surfaces.10,11 AIDS's very advanced stage causes low levels of CD4+ cells, leading to a subsequent decrease in the production of IL-17 and IL-22, and AMPs fail to form in turn C. Albicans transform from normal flora to pathogens and manifest in the oral cavity.12

Oropharyngeal Candidiasis is an oral manifestation due to very low levels of CD4 cells.12 Based on clinical examination, the appearance of oral CAD can vary, with pseudomembranous candidiasis or thrush being the most commonly observed manifestations.13 Thrush is characterized by white patches on the oral mucosa, tongue, or other anatomical regions of the body.13 The lesions have confluent plaques that bear a resemblance to milk curds.13 These plaques reveal a raw, erythematous, and sporadically bleeding base upon removal.13 Oropharyngeal Candidiasis is frequently observed in individuals at advanced stages of HIV infection, commonly known as AIDS.14 This condition can manifest through a range of symptoms, such as white patches on the inner cheeks, tongue, palate, and throat, accompanied by redness or discomfort.15 Additionally, individuals may experience a cottony sensation in the mouth, a diminished sense of taste, pain while eating or swallowing, and cracking and redness at the corners of the mouth.

Candida yeast is commonly found in immunocompetent individuals, often as a component of healthy individuals' commensal microorganisms in the oral cavity, intestines, and skin.16-18 The growth of Candida is typically constrained by the human immune system and by the presence of other microorganisms, which engage in competitive interactions.6 C. albicans, the predominant yeast species in the oral cavity, exhibit pleomorphism, displaying several development forms, including rod-shaped cells, yeast (blastopore) cells, hyphae or pseudohyphae, and chlamydotheciae.19

The hyphal morphology is commonly regarded as the invasive state of the fungus, facilitating the ability of C. albicans to breach host barriers and infiltrate deep-seated tissues.18 Many virulence factors modulate the infectivity of Candida.18 The expression of virulence factors in C. albicans is modulated by the processes of adhesion and invasion.20 These processes are facilitated by ALs3 and Ssa1, genes found in C. albicans.20 ALs3 and Ssa1 interact with E-cadherin and epidermal growth factor receptors (Egfr), which are present in oral epithelial cells.20 The binding of ALs3 and Ssa1 to these receptors induces the endocytosis of C. albicans hyphae.20

The synthesis of secreted aspartic proteinases (Saps), which are hypha-associated proteins, occurs simultaneously with hyphae formation.21 These Saps are crucial in inducing epithelial cell damage and enhancing fungal virulence.21 Additionally, they facilitate the recruitment of neutrophils and promote the production of pro-inflammatory cytokines such as IL-1β and TNF-α.21

Due to the severity of the AIDS stage, 2-layer therapy oropharyngeal candidiasis is given to prevent the infection from getting worse. In the first layer, topical therapy was given as antiseptic chlorhexidine in gluconate, 0.2%, and antifungal oral nystatin, 100,000 IU/ml. The second layer of systemic therapy is fluconazole injection at 2 mg/ml.

Chlorhexidine digluconate is a type of antifungal agent that falls under bisbiguanade antimicrobials.22 It is frequently utilized in its gluconate formulation. Chlorhexidine is an antimicrobial agent with a wide range of effectiveness against gram-positive and gram-negative bacteria, yeast, fungus, protozoa, algae, and viruses.22 Antifungal agents exert their action by disrupting the permeability of cell wall membranes and
extracellular proteins, specifically in *C. albicans* fungi.\(^2^3\)

The *chlorhexidine* formula is often the preferred choice, consisting of a biguanide substitution (N1, N5) attached to *hexamethylene*, with two chlorophenol rings positioned at either terminus.\(^2^2\) At lower concentrations, *chlorhexidine* disrupts cellular transport, leading to the creation of holes in the cellular membrane, which subsequently results in damage to fungal cells.\(^2^2\) *Chlorhexidine digluconate* at a concentration of 0.2% has antiseptic properties, effectively targeting bacteria and fungi.\(^2^2\) The efficacy of a 0.2% chlorhexidine digluconate solution in inhibiting the development of microorganisms, particularly Candida albicans, has been demonstrated through empirical evidence.\(^2^2\) Additionally, this solution has exhibited a notable inhibitory effect on many fungal species, as evidenced by a substantial zone of inhibition.\(^2^3\),\(^2^2\)

The classification of anti-fungal therapy encompasses three distinct categories: The three classes of compounds discussed are polyenes, azoles, and pyrimidines.\(^1\) Nystatin is classified as a polyene antifungal agent, which exerts its mechanism of action by selectively attaching to sterol structures present in the cell membranes of fungi, particularly ergosterol.\(^2^4\) This binding event leads to a notable elevation in cell permeability, resulting in the leaking of intracellular molecules.\(^7\)

**CONCLUSION**

The oral lesions associated with HIV were commonly considered significant indicators and markers of HIV/AIDS. The Decrease in CD4\(^+\) in HIV/AIDS condition also decreased the amount of IL-17 and IL-22, which were cytokines that induced the secretion of local innate immunity cells in the oral cavity (*ß-Defensin, S100A8/A9, and Histatin*) which in turn led to susceptibility of the oral mucosa epithelium and provided a suitable environment for the transformation of *C. albicans* from commensal microbiome to pathogenic.

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**REFERENCES**


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