Introduction

Oral candidiasis is the most common fungal infection of the oral cavity, and is a common presentation in very young, old and sick persons. The most common Candida species isolated from the oral cavity both in health and disease is the Candida albicans, followed by C. tropicalis, C. glabrata, C. parapsilosis, and C. krusei. Candida albicans is one of the dimorphic fungus existing both in yeast phase and hyphal or mycelial phase. Yeast is innocuous form while hyphal forms are associated with invasion of host tissue. Entry of these commensals into the deeper tissues results when the host defenses are compromised. Candida species of major medical importance are C. albicans, C. tropicalis, and C. glabrata which are most frequently isolated (more than 80%) from medical specimens. The reported prevalence in clinically normal mouths of healthy adults ranges from 3 to 48%, and 45 to 65% of healthy children. The term candidiasis and candidosis are both used to describe the lesions. However, the term “Candidosis" is more commonly used in the United Kingdom and Europe and is used to describe lesions of the oral cavity, while "Candidiasis" is used more often in the United States and denotes general effects caused by the fungus. In the present article is used the term candidiasis.

Case report

A 75 year old male patient reported to the institution for replacement of his missing teeth. The patient was completely edentulous and had history of smoking beedis for the past 40 years about 1 pack per day. Intraoral examination revealed white patches present bilaterally on the buccal mucosa (Figure 1) with cracked mud surface appearance. The buccal mucosal lesions were measuring approximately 2 cm in size from retrocommisural area, non scrapable and nontender. Examination of the tongue revealed brownish coating (Figure 2) and angular cheilitis was also noted (Figure 3). Diffuse black to brown pigmentation of oral mucosa was also evident. The patient was completely asymptomatic at initial presentation. On subsequent visit the patient complained of burning sensation at the corner of the mouth. Considering his clinical presentation and positive tobacco history a provisional diagnosis of leukoplakia of bilateral buccal mucosa and angular cheilitis was made.

Routine hematological examination conducted was normal except for the decreased hemoglobin percentage and elevated erythrocyte sedimentation rate, Tridot test for Human Immunodeficiency Virus (HIV) was negative. Exfoliative cytologic smears were prepared from the buccal mucosa and from the lesion at the corner of the mouth. Cytosmears stained with Per Iodice acid Schiff and Papanicolaou stain revealed numerous yeast and branching hyphal forms of septate fungus (Figure 4, 5). Incisional biopsy was performed from the buccal mucosa to rule out dysplasia. Hematoxylin and eosin stained tissue from the same showed mild epithelial dysplasia.

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Candidiasis - A frequently underdiagnosed entity

Discussion

Candida albicans is a commensal of the oral cavity. Overgrowth of the fungus Candida results in Oral candidiasis. In general population the carriage rates have been reported to range from 20% to 75% of the population without any symptoms.6 The presence of C albicans has been detected in the oral cavity of 45% neonates, 45%–65% healthy children, 30%–45% of healthy adults, 50%–65% of people with removable dentures, 65%–88% in those residing in long term care facilities, 90% of patients undergoing chemotherapy for acute leukemia, and 95% of HIV infected individuals.7-14

Candidal infection has been associated with numerous pathologic variables. Initiation of infection is brought about by the adhesion of candida to epithelial cell walls by certain fungal cell wall components such as mannose, C3d receptors, mannoprotein, and saccharins. In the initial stages of infection the degree of hydrophobicity and ability of the fungus to bind to host fibronectin are also important. Germ tube formation, presence of mycelia, persistence within epithelial cells, endotoxins, induction of tumor necrosis factor, and proteinases are other factors which are implicated. The ability of certain strains of C albicans to change between different morphologic phenotypes called as “phenotypic switching” has also been implicated in the pathogenicity.15

A yeast or the blastospore is a unicellular form of the fungus that divides by budding. A hypha comprises multiple fungal cell units divided by septa. Germ tube formation is the initial stage in yeast – hyphal transition.15 Transformation from the yeast to hyphal form takes place when temperature and pH alterations occur within the host. The yeast growth is favoured when the host temperature is below 33°C and when pH turns acidic (average pH = 4). As the pH becomes neutral and temperature increases to 37°C hyphal growth occurs. Pseudohyphae are produced between these temperatures. The quorum sensing molecules produced by the resident oral bacteria like S. mutans and S. gordonii are capable of promoting or attenuating the hyphal growth.16
Candida carriage and related factors

Numerous factors affect the carriage of candida in the oral cavity. Carriage is more frequent in females than males, and mostly during summer months. In patients with xerostomia there is increased tendency for candidal carriage due to lack of flushing action of saliva, and absence of antifungal salivary constituents such as lactoferrin and lysozyme. Correlation between the pH of the surface and Candida carrier status have shown that the carriage of yeast is higher in acidic saliva. Studies have shown the counts to be highest during early morning. During sleep the count increases and are reduced by tooth brushing and by taking meals.1

Numerous hypotheses have been put forward to link candidal colonization with smoking. Localized epithelial alterations caused by cigarette smoking is thought to allow colonization by Candida or the smoking itself provides nutrition for C. albicans.4 Certain species of candida such as C. tropicalis, C. guilliermondii, and C. pulcherrima replicate by their inducible enzyme systems using polycyclic aromatic hydrocarbons as their source of carbon and energy.17 Where as few studies have shown no impact of betel quid chewing on oral colonization by candida species.18 Posterior dorsum of the tongue is the main site of candidal colonization. Persons of blood group ‘O’ and nonsecretors of blood group antigens in saliva shows greater carriage of candida. Carriage rate are also influenced by specific antibodies to C. albicans and decreasing T-lymphocyte helper-to-suppressor ratios.19-21

Factors which predispose to oral candidiasis may be related to prostheses, ill fitting appliances, inadequate care of appliances, abnormal nutrition, age, smoking, immunological and endocrine disorders, malignant and chronic diseases, radiation to head and neck, severe blood dyscrasias, hospitalization, oral epithelial dysplasia1, and also a positive correlation has been established between poor oral hygiene and the presence of candida species.22 In our case it might be related to advanced age, reduced vertical dimension of the mouth, smoking and poor nutritional status of the patient.

Classification

Oral candidiasis is mainly classified in to primary and secondary infections as shown in Table 1.2,23 In the initial stages of infection there is adhesion of the candida to the epithelium and acquisition of the nutrition. The second stage comprises superficial infection which is characterized by epithelial penetration and degradation of host proteins followed by deep seated infection in which there is tissue penetration, vascular invasion and immune evasion or escape this may later lead to disseminated infection which includes endothelial adhesion, infection of other host tissue, and activation of coagulation cascade.16

<table>
<thead>
<tr>
<th>Table 1: Classification of oral candidiasis2,23</th>
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<tbody>
<tr>
<td><strong>Primary oral candidiasis</strong></td>
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<tr>
<td>a. Acute form</td>
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<tr>
<td>i. Pseudomembranous</td>
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<tr>
<td>ii. Erythematous</td>
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<tr>
<td>b. Chronic form</td>
</tr>
<tr>
<td>i. Erythematous</td>
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<tr>
<td>ii. Pseudomembranous</td>
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<tr>
<td>iii. Plaque like</td>
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<td>iv. Nodular</td>
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<tr>
<td>c. Candida associated lesions</td>
</tr>
<tr>
<td>i. Denture stomatitis</td>
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<tr>
<td>ii. Angular cheilitis</td>
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<tr>
<td>iii. Median rhomboid glossitis</td>
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<tr>
<td><strong>Secondary oral candidiasis</strong></td>
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<td>a. Oral manifestation of systemic mucocutaneous candidiasis</td>
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<tr>
<td>i. Familial mucocutaneous candidiasis</td>
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<td>ii. Diffuse chronic mucocutaneous candidiasis</td>
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<tr>
<td>iii. Familial mucocutaneous candidiasis</td>
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<td>iv. Chronic granulomatous disease</td>
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<td>v. Candidias endocrinopathy syndrome</td>
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<td>vi. Acquired immune deficiency syndrome (AIDS)</td>
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Differential diagnosis

Many lesions of oral mucosa can present as white lesions, commonest being candidiasis, leukoplakia, lichen planus, frictional keratosis, leukedema, chemical burns and white sponge nevus. Few of these lesions like candidiasis, chemical burn are scrapable, while the rest are often nonscrapable. The present case reported with bilateral white lesions on the buccal mucosa in the retrocommissural area along with coated tongue however the patient was asymptomatic and unaware of the condition. A positive tobacco usage history and old age prompted a provisional clinical diagnosis of homogenous leukoplakia of buccal mucosa with subsequent biopsy performed from left buccal mucosa. However, histopathologic examination revealed mild dysplasia. On subsequent recall cytomsears from buccal mucosa and angle of the mouth were obtained which revealed numerous candidial colonies which were unnoticed during initial presentation.

Angular stomatitis also called as Perleche or Angular Cheilitis affects the angles of the mouth causing erythema, fissuring and soreness. Predisposing factors includes both yeast and bacteria. At times it might be an early sign of anemia and vitamin deficiency. Edentulous individuals, HIV infected persons, and 20% of individuals with orofacial granulomatosis present with angular cheilitis. The lesion is thought to occur as a result of maceration due to deep, occlusive folds of skin at the mouth angles in individuals with reduced facial height as a result of old age or edentulous arch.1 60% of the cases are related to mixed candidal bacterial infections, 20% related to candidiasis and 20% bacterial infection alone.24 In the present case the decreased vertical dimension of the mouth with resultant stagnation of saliva at the corner of the mouth may be the cause for angular cheilitis.
Malignant potential
The role of candida in the causation of oral cancer is controversial. Carcinogenesis may be related to candida species elaborating nitrosamine compounds, which then act directly on the oral mucosa or interact with other chemical carcinogens there by activating specified protooncogenes to initiate oral neoplasia. The hydrocarbons in the cigarette smoke can induce the enzyme systems of the candida which increase the carcinogenic activity of the hydrocarbon and hence candidal leukoplakia might have a higher potential for malignant changes than other leukoplakias. In nonhomogeneous leukoplakia the candidal types differ and they are thought to have higher nitrosoation potentials than others, which might indicate a possible role of specific types in the transformation of some leukoplakias.1 Malignant transformation is mostly seen in chronic plaque and nodular types of candidiasis.1,2

Diagnosis
Thorough oral examination and related history are the initial step for the diagnosis. Diagnosis is mainly based on clinical signs and symptoms, a positive cytological smear, staining with 10% potassium hydroxide, culture with Sabouraud’s dextrose agar, germ tube test and tissue biopsy. Candidal count more than 400CFU/ml of saliva are predictive of oral candidiasis.2,24-26 And there is an indication for biopsy in hyperplastic candidiasis cases. Also individual species of candida can be identified with CHROMagar Candida® culture. For the diagnosis of different species of candida immunological and genetic techniques such as enzyme linked immuno sorbent assay and polymerase chain reaction can also be used.26

Treatment
Several antifungal agents can be used to topically treat oral candidiasis. Topical agents include nystatin suspension and clotrimazole troches used five times daily for 14 days.2 For topical agents adequate contact time of 2 minutes with the oral mucosa is required. Therapy should be continued for 2 to 3 days beyond the last clinical signs and symptoms.21 Other drugs such as Clotrimazole can be taken as lozenges and Amphotericin B as oral suspension. For severe, localized, immunosuppressed patients and patients who respond poorly to primary line of treatment second line of drugs such as Ketoconazole, Fluconazole and Itraconazole can be used.4 The present case was advised topical antifungal mouth wash and regular follow up.

Conclusion
All white lesions of the oral cavity have to be viewed with suspicion. Candidiasis is quite common oral lesion but it is mostly not thought of as first choice especially if there is a positive tobacco history. Hence keen observation, complete history along with few chair side tests are a must in such a case.

References
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Ashwini et al


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