

Prevalence of Candida Species in oral cavity during radiation therapy in Oral cancer patients

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Abstract

Background: It is observed that during the course of radiotherapy many patients of oral cancer develop many changes in the oral cavity due to effects of radiation. There is increase in candida infection in oral cavity which may be attributed to radiation induced xerostomia. Reduced salivary production can predispose patients to oral candidiasis as salivary constituents inhibit the overgrowth of candida, as radiation reduces the amount and characteristics of saliva secretion leading to candida overgrowth. There is an increased rate of candida infection associated with neutropenia also. **Objective and hypothesis:** The objective of this study was to investigate the prevalence of candida species in oral cavity of patients of oral cancer during the course of radiotherapy. **Methods:** We collected samples using two swabs from 40 patients of oral cancer who developed oral lesions suggestive of candidiasis, while undergoing radiotherapy treatment. **Results:** In this study Candida species isolated from oral cavity lesions clinically diagnosed as Candidiasis from the patients undergoing radiotherapy were Candida albicans - 28 (70%) was the predominant species isolated followed by Candida dubliniensis 4 (10%), C. tropicalis was isolated in 3 (7.5%) of the samples, C. krusei - 2 (5%), C. guilliermondii, C. parapsilosis, C. glabrata were found in 1 (2.5%) patient each. **Conclusion:** Oropharyngeal candidiasis is a common fungal infection in patients undergoing radiation treatment. Clinical signs and symptoms and microbiological studies will help us in early diagnosis. There are several practical considerations which patients can take to reduce the risk of such infections.

Keywords: Candidiasis, radiotherapy, oral cancers

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Introduction

Patients of oral cancers undergoing radiotherapy were seen to develop oropharyngeal candidiasis. This increase in candida infection may also be attributed to radiation induced xerostomia[1]. Due to xerostomia, there is damage to the plasma membrane of the acinar cells of salivary glands. The cell regeneration often cannot match with the rate of cell death resulting mucosal damage[2]. Reduced salivary production can predispose patient to oral candidiasis as salivary constituents inhibit the overgrowth of candida, as radiation reduces the amount and characteristics of saliva secretion which leads to candida overgrowth. Xerostomia does not only mean that there is reduction in saliva flow but it may also present as independent of hyposalivation. Daily production of saliva in a normal healthy adult is estimated to be about 500ml – 1500ml. Three paired major salivary glands are mainly responsible for production of saliva. Saliva is made up of 99% water and 1% protein and salt. Salivary glands are very sensitive to radiation, it damages the acinar and ductal system and the damage is directly proportional to the radiation dose received by the salivary gland and the volume of the gland included in the radiation fields. Radiation changes the volume of salivary secretion as well as its constituents by increasing its salt content and decreasing its water content. Candida species are the component of normal flora of human being. This has been observed that most of the times it has been found as an

indigenous infection due to its commensal nature. A variety of factors are known to predispose both superficial and deep-seated candidiasis. All these factors act either by altering the balance of normal microbial flora of the body or by lowering the host resistance. Mostly numerous factors operate collectively and full-fledged infection takes place. Although candida albicans remain the most common causative agent of oropharyngeal candidiasis but other species of non-albicans candida such as C. dubliniensis, C. krusei, C. guilliermondii were also documented[3]. As such immune response to candida species is basically shaped by its commensal character. The classical T-cell mediated immunity is important in protection from persistent high level mucocutaneous Candida colonization. A variety of systems are operative to augment the function of these effector cells. Serum factors, the complement system and antibody may serve this function in part. Additionally, augmentation of phagocytic cell function appears to occur by activity of NK cells and immune T-cells mediated primarily by the cytokines IFN and TNF. Early in infection or in hosts with impaired T-cell function NK cell may be the primary source of such cytokines. When yeast cells of Candida penetrate mucus membrane ultimate effectors of destruction of organism are phagocytic cells. These cells provide phagocytic and candidacidal activity following fungal penetration. There is an increased rate of candida infection associated with neutropenia. This leads to symptoms such as altered taste and dysphagia leading to poor nutrition and prolonged hospital stay. In immunocompromised patients it causes more severe infections.

Material and Methods

From the patients of oral cancer undergoing radiation treatment at the Department of Radiotherapy, Patna Medical College, Patna, India, 40

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patients who developed white plaque, erythematous lesions, ulcerative lesions, dryness of mouth, oral pain, altered taste sensation who were clinically diagnosed as suspected oropharyngeal candidiasis were enrolled in this study between March 2020 to February 2021. Unwillingness to participate and patient on antifungal therapy for the past two weeks were excluded from the study. The study was explained and informed consent were taken from the patients. Processing of the samples were done in the Department of Microbiology, Patna Medical College, Patna, India. Two sterile swabs were used to collect sample from the oral cavity by swabbing from the lesion. One swab was used for direct Gram staining and direct microscopy with 10% KOH in which candida was present with budding yeast cell (blastocoonidia 2 to 4 um in diameter and/ or pseudo hyphae showing regular points of constriction resembling link of sausage were present. And blastocoonidia, hyphae and pseudo hyphae were strongly gram positive.) Other swab was used for inoculating the specimen in Sabouraud dextrose agar (SDA) and

CHROMagar Candida medium. The growth that was inoculated in SDA was incubated at 24°C for 48 hours. The growth of creamy white colony was subjected to Gram staining for presence of gram-positive budding yeast cells. Germ tube test was performed for all the isolates. In the germ tube test, it appeared as hyphal like extension of yeast cells that were produced without a constriction at the point of origin. The candida albicans and candida dubliniensis showed positive germ tube test. And further specialization was done by colony morphology and in chrome agar (color of the colony) and sugar assimilation test and fermentation test as per standard microbiological technique. CHROMagar is a rapid plate-based test for the simultaneous isolation and identification of various candida species. This is a relatively new medium that distinguishes different candida species by color as a result of biochemical reaction. It was incubated for 24-48 hours at 37 degrees centigrade. According to the different color produced in the CHROMagar media different species of candida was identified.

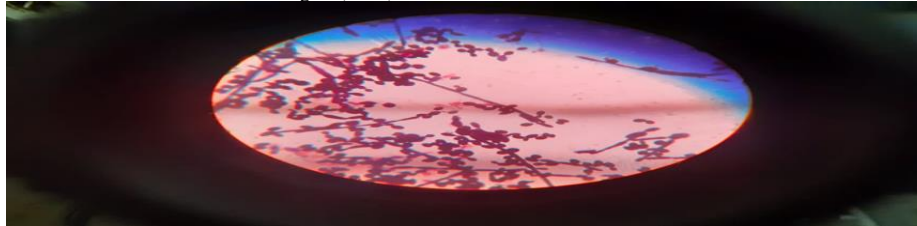


Fig 1: Budding Yeast Cell with pseudo hyphae seen in Gram Staining. – Candida Species.

Results

In this study Candida species isolated from oral cavity lesions clinically diagnosed as Candidiasis from the patients undergoing radiotherapy were Candida albicans - 28 (70%) was the predominant species isolated followed by Candida dubliniensis 4(10%), C. tropicalis was isolated in 3(7.5%) of the samples, C. krusei - 2 (5%), C. guilliaermondii, C. parapsilosis, C. glabrata were found in 1 (2.5%) patient each.

- C. albicans -28 (70%)
- C. dubliniensis-4(10%)
- C. tropicalis-3(7.5%)
- C. krusei- 2 (5%)
- C. guilliaermondii-1(2.5%)
- C. parapsilosis-1 (2.5%)
- C. glabrata-1(2.5%)

Discussion

Oropharyngeal candidiasis is a major problem in the patients undergoing radiotherapy treatment. Patients usually progress from asymptomatic colonization to infection. Radiotherapy decreases the immunity and increases the risk of candida infections. Radiation leads to decrease in quantity and changes the quality of saliva[4]. Dryness of mouth and pain in the oral cavity are the most frequently encountered symptoms. In the present study we found out that there

was a significant association between presence of dry mouth and isolation of candida species. Candida albicans - 28 (70%) was the predominant species isolated followed by Candida dubliniensis 4(10%), C. tropicalis was isolated in 3(7.5%) of the samples, C. krusei - 2 (5%), C. guilliaermondii, C. parapsilosis, C. glabrata were found in 1(2.5%) patient each, which is in accordance with previous studies [5]. Non candida albicans as found in this study 30% is similar to those found in the patients receiving radiotherapy in study conducted by Dahiya MC et. al[6] Studies have reported that development of candidiasis is a two-step process consisting of colonization and subsequent invasion of epithelial layer. Once colonization has been established, impaired cellular immunity persists invasion of epithelial layer⁷. Neutropenia, irradiation will lead to mucosal disruption facilitating deeper invasion by candida. Maintenance of adequate nutrition and hydration is very important aspect of oral care during radiation therapy[8], using saline oral rinsing, medicated mouth wash or salivary substitutes can help[9]. Radiation damages the salivary glands by generating free radicals so prescribing antioxidants to these patients decreases the toxic effect of radiation to healthy cells. It is well known that salivation is stimulated by mastication, so the patients experiencing xerostomia be encouraged for chewing foods properly and doing chewing exercises[9].





Fig 2: White plaque, Erythematous lesions, Ulcerative lesions, Oral Thrush

Conclusions

Oropharyngeal candidiasis is a common fungal infection in patients undergoing radiation treatment. Clinical signs and symptoms and microbiological studies will help us in early diagnosis and timely management. There are several practical considerations which patients can take to reduce the risk of such infections. Rinsing mouth out after eating, taking medications or using a corticosteroid inhaler. Good oral hygiene, brushing teeth twice per day using soft tooth brushes. Going for regular dental check-ups even if patients do not have any teeth.

References

1. Cooper JS, Fu K, Silverman S. Late effects of radiation therapy in the head and neck region. *Int J Radiat Oncol Biol Phys.* 1995; 31:1141-64
2. Dental complications of head and neck radiotherapy: Part 2 Nectarios Andrews, Chris Griffiths Samaranayake LP. *Oral mycoses in HIV infection.* *Oral Surg Oral Med Oral Pathol.* 1992;73:171-80
3. Dreizen S, Brown L, Daly T et al. Prevention of xerostomia related dental caries in irradiated cancer patients. *J Dent Res.* 1977;56:99
4. Silverman S, Luangjarmekorn L, Greenspan D. Occurrence of oral candida in irradiated head and neck cancer patients. *J oral Med.* 1984;39:194-6
5. Dahiya MC, Redding SW, Dahiya RS, Eng TY, Kirkpatrick WR, Coco BJ et al. Oropharyngeal candidiasis caused by non-albicans yeast in patients receiving external beam radiotherapy for head-neck cancer. *Int. J Radiat Oncol Biol Phys.* 2003; 57:79-83.
6. Sonis ST. A biological approach to mucositis. *J Support Oncol.* 2004; 2:21-36
7. Lynch DP. Oral candidiasis. History, classification and clinical presentation. *Oral Surg Oral Med Oral Pathol.* 1994; 78(2):189-93
8. Jacob R. Management of xerostomia in the irradiated patient. *Clin Plast Surg.* 1993;6:243.
9. Coial L, Moylan D. *Introduction to Clinical Radiation Oncology*, Medical Physics Publishing Company, Copyright, 1991, 4.

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