



Mycological species of Central Papillary Atrophy (CPA)

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Abstract

Background: Central Papillary Atrophy (CPA) is a chronic candidal infection at the dorsum of the tongue, at which different candidal strains are frequently isolated. **Aims:** This study aimed to determine the microbiological makeup in the routine dental patients clinically diagnosed with this condition to assess any association between the type of candida species in the isolate and systemic diseases encountered in those patients. **Material and Methods:** The susceptibility of the isolates to different therapeutic agents of the isolated fungal species was also assessed. The study sample comprised 62 isolates from the tongue of 34 males and 28; with an age range of 5 to 72 years subjected to mycological examination with the standard international laboratory methods. **Results:** Different Candida species were isolated from 51.6% of CPA patients (mostly seen in the age group 51–60 years), their mycological examination without any statistically significant correlation between the candida strains and systemic disorders or drugs taken by CPA patients do not show. McFarland turbidity standards were used to standardize the approximate number of fungi in a liquid suspension. The susceptibility to antifungals as tested by the Kirby-Bauer method and a fully automated VITEK[®] system was used to perform candidal identification. **Conclusion:** CPA is a unique and uncommon condition affecting the tongue containing numerous microbats. There is a significant correlation between denture-wearing and candidal strains in CPA lesions and susceptibility to different antifungal agents.

Keywords: CPA, candida, antifungal susceptibility, VITEK 2[®] system.

Introduction

Central Papillary atrophy (CPA) is a rare benign inflammatory anomaly of the tongue that usually appears as a reddish, rhomboid depapillated patch at the midline of the dorsum of tongue, anterior to the lingual "V" line ¹. The condition is typically asymptomatic and can only be noticed upon routine oral tongue examination ². It is believed to be caused by oral candidal infection abetted by more than a few predisposing factors such as diabetes mellitus ^{3,4}, denture wearing ⁵, and smoking (although it seems to be as common in smokers as it is in non-smokers) ⁶. *Candida albicans* is the most frequently isolated species from CPA lesions, nonetheless, other candidal species were also isolated to a lesser extent.

The scarce long-term follow-up studies of this condition ensued by its relative low frequency and its benign and asymptomatic nature, however, the microbiota of CPA were extensively studied and their susceptibility to various therapeutics were evaluated. This study investigates the relationship between CPA and the fungal species, and any possible relation with age, gender, smoking, denture wearing, and other systemic diseases such as diabetes mellitus. No treatment is necessary; but if the lesion is painful, a topical antifungal agent may be indicated ¹.

Materials and Methods

Clinically identified 62 dental patients positively diagnosed with CPA, (34 males and 28 females their ages ranged from 5 to 72 years) were interviewed and comprehensively examined in the dental clinic and a swab was taken by sterile cotton swabs collected from multiple regions of the lesion and immediately transferred to the laboratory. Tongue cultures were subjected to mycological examinations, for fungal cultivation it was on Sabouraud dextrose agar (SDA), incubated at 37°C for 48 hours, colonies were examined for their shape, size, color and stained with gram stain and lactophenol cotton blue stain, and then tested by germ tube test (GTT) to confirm the existence of *C. albicans* species, VITEK® semi-automated system was used to perform candidal identification test. The susceptibility to antifungals (Nystatin, Miconazole Voriconazole, Fluconazole, Itraconazole, Clotrimazole, Amphotericin-B, and Flucytosine) was tested by Kirby- Bauer method. McFarland turbidity standards were used to standardize the approximate number of isolated fungi in a liquid suspension.

Results

Among the 62 cases, there was an almost equal number of males and females in this study (32

males and 28 females), all of them presented with asymptomatic lesions except for 6 patients who reported mild tongue soreness. The reported systemic diseases in this group included diabetes mellitus, hypertension, chronic sinusitis, peptic ulcer, and bronchial asthma to which these patients were using medications, but there was no statistically significant correlation between any of these diseases or medications and the type of the isolated candida strain. The majority of patients are non-smokers 35 (56.5%) patients, while 18 (29%) are smokers and 9 (14.5%) are ex-smokers without any statistically significant correlation between smoking and the type of candida species. There were 6 denture wearers with a significant correlation of that with the type of candidal strains in CPA lesions.

There were 32 (51.6%) positive isolates of *Candida* Spp. and 30 (48.4%) negative isolates. The fungal strains identified are 27 *C. albicans*, 3 *C. glabrata* and 1 *C. tropicalis* and 1 *C. dubliniensis*. Moreover, in the 27 cases of *C. albicans* isolates in this study, there were 21 positive reactions of germ tube test (GTT) Figure (4), to which no other strain was positive in Table (2). Moreover, *C. albicans* was the only strain that isolated in young age groups (1- 30 years), while the others could only be found in the older age groups.

Regarding the antifungal sensitivity test, all candida isolates in this study were sensitive to miconazole 32 (100%), then to Voriconazole 28 (78.5%), fluconazole 27 (84.3%), Itraconazole 24 (75.0%) and nystatin 22 (68.7%). Whereas there was less susceptibility to clotrimazole 6 (18.7%) and some extent amphotericin-B and complete resistance to Flucytosine table (3). On contrary, no reported resistance to neither nystatin nor miconazole. Other agents, however, had variable fungi susceptibility and it was mostly of intermediate degree.

Discussion

Due to its benign nature, CPA, seldom catch great attention or needs any active treatment has resulted in paucity of research about it ^{1,2,3}. Occasionally patients may report local numbness or burning sensation of the affected area of the tongue ⁴. CPA rarely can have any significant impact on the person's ability to enjoy food or alter their eating habits or the overall quality of life ⁵. The most acceptable theory nowadays for the etiology of CPA is an overgrowth of the fungus *Candida*, particularly *C. albicans* which is the most frequently isolated species ⁶. This is apparently augmented by other predisposing factors such as local irritation, chronic antibiotic use, immunosuppression, smoking, and denture wearing which can create a favorable environment for *Candida* organism to change itself from a commensal microorganism to a pathological one. The presence of some types of bacteria can help the candida organisms to overgrow and assist in the development of CPA ^{6,7}.

In a study, a lesion was more predominant in males than females. It has been widely argued that

this lesion is not a developmental disorder but a clinical manifestation of a fungal etiology ¹⁵.

Candida genus-related fungi particularly *Candida albicans*, are significant contributors to the oral cavity's microbiota. The process of microbial colonization in the oral cavity is closely linked to the development of multispecies biofilm, on dental and denture plaque ⁷. The most significant species of *Candida* thought to be capable of causing oral infections in people who wear dentures is *Candida albicans*. *C. dubliniensis* has become known as a harmful yeast to humans in recent years. In patients with denture-related stomatitis (DRS) or not, *C. dubliniensis* was identified at low rates from palate and maxillary denture samples. Nonetheless, *C. dubliniensis* was consistently linked to *C. albicans* when it was found in people with DRS ⁸. It is determined that primary cancer on the tongue's dorsum is an uncommon occurrence. It can be mistakenly identified as granular cell myoblastoma, median rhomboid glossitis, or any other lesion related to pseudoepitheliomatous hyperplasia. When analyzing lesions in this region, these conditions should always be taken into account. Even though histological diagnosis is challenging, it can be considerably aided by appropriate biopsy methods. However, to prevent these diagnostic errors, excellent communication between the pathologist, radiotherapist, and surgeon is crucial ⁹. There was a statistically significant relationship between the presence of candidal mycelia in smears from these tongue lesions and the use of removable dental prostheses. It does not seem that atrophy of the papillae of the middle part of the tongue-dorsum is predisposed by general age changes ¹⁰. The type of candida strains in the isolates in the current study were similar to those of other worldwide studies and constituted predominantly *C. albicans*, and to a lesser extent *C. tropicalis*, *C. glabrata* and *C. dubliniensis*. Except for denture wearing no other suggested predisposing factors have any relation to the type of candida strain. It is well known fact that there are irregularities in the outcome of treatment of CPA with antifungal agents which questions the full responsibility of candida Spp as the sole cause of CPA and the important role of other predisposing factors in that. Many recent studies provided evidence of an interaction between some types of bacteria and *Candida* leading to major influences in the ability of its virulence, pathogenicity, adherence, and antifungal susceptibility.

CPA is a unique and uncommon condition that affects the tongue. While its etiology remains unclear, careful clinical examination and diagnostic tests can aid in its identification. Management primarily focuses on symptomatic relief and addressing potential underlying conditions, In addition to the role of nutritional supplements, which was helpful in some instances, especially if the underlying illness is treated, leading to the atrophic tongue lesion to subside. Nutritional deficiency of importance in this regard is frequently linked to an iron, folic acid, vitamin B12, riboflavin, or niacin nutritional deficiency ⁽¹⁶⁾.

Continued research and collaboration with other centers are necessary to improve our understanding of this condition and its implications for oral and systemic health.



Figure 1: CPA lesion in middle aged male patient

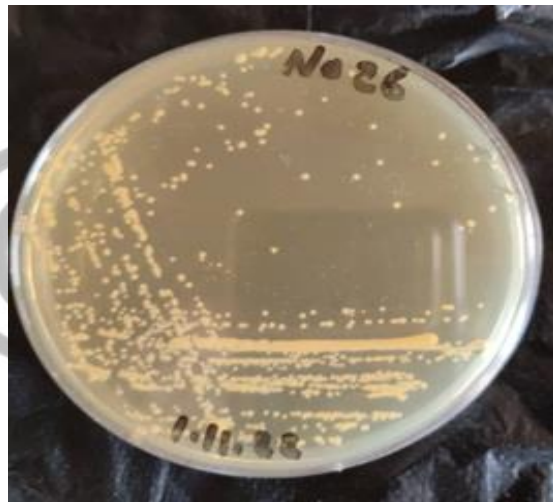


Figure 2: Positive candida growth on Sabouraud dextrose agar (SDA)

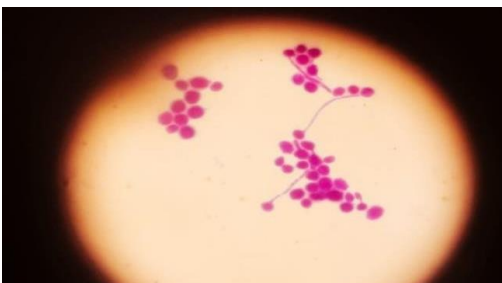


Figure 4: positive reactions of germ tube test

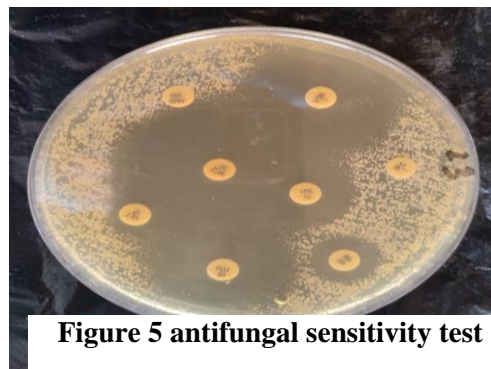


Figure 5 antifungal sensitivity test

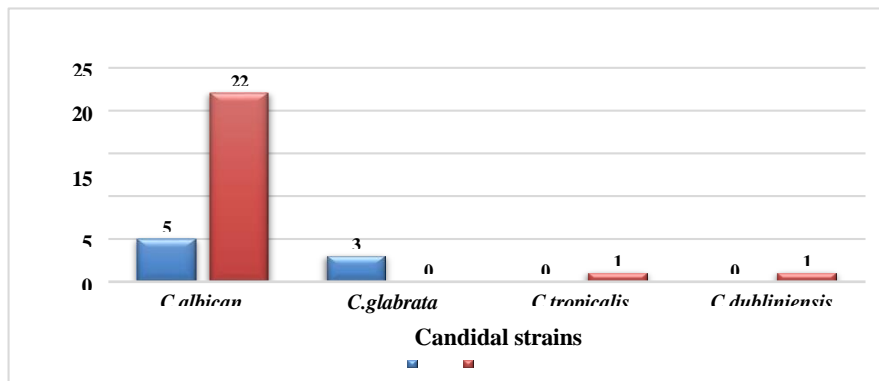


Figure 3: Candida strains in denture wearers

Table 1: Susceptibility of different candida species to antifungal agents

Candida strain	Nystatin (100 IU)			Clotrimazole (10 mg)			Flucytosine (10 mcg)			Voriconazole (1mcg)			Itraconazole (10 mcg)			Fluconazole (10 mcg)			Miconazole (50mcg)		
	R*	I	S*	R	I	S	R	I	S	R	I	S	R	I	S	R	I	S	R	I	S
<i>C.albicans</i>	0	9	18	21	5	1	27	0	0	2	0	25	2	3	22	1	2	24	0	0	27
<i>C.glabrata</i>	0	0	3	3	0	0	3	0	0	2	0	1	2	0	1	1	1	1	0	0	3
<i>C.tropicalis</i>	0	1	0	1	0	0	1	0	0	0	0	1	0	1	0	0	0	1	0	0	1
<i>C.dubliniensis</i>	0	0	1	0	1	0	1	0	0	0	0	1	0	0	1	0	0	1	0	0	1

References

1. Banoczy J, Rigo O, Albrecht M. Prevalence study of tongue lesions in a Hungarian population. *Community Dent Oral Epidemiol.* 1993;21(4):224-6.
2. Farman AG, van Wyk CW, Staz J, Hugo M, Dreyer WP. Central papillary atrophy of the tongue. *Oral Surg Oral Med Oral Pathol.* 1977;43(1):48-58.
3. McNally MA, Langlais RP. Conditions peculiar to the tongue. *Dermatologic clinics.* 1996;14(2):257-72.
4. Espinoza I, Rojas R, Aranda W, Gamonal J. Prevalence of oral mucosal lesions in elderly people in Santiago, Chile. *J Oral Pathol Med.* 2003;32(10):571-5.
5. Soysa NS, Ellepola AN. The impact of cigarette/tobacco smoking on oral candidosis: an overview. *Oral Dis.* 2005;11(5):268-73.

6. Goregen M, Miloglu O, Buyukkurt MC, Caglayan F, Aktas AE. Median rhomboid glossitis: a clinical and microbiological study. *Eur J Dent.* 2011;5(4):367-72.
7. van der Wal N, van der Kwast WA, van der Waal I. Median rhomboid glossitis. A follow-up study of 16 patients. *J Oral Med.* 1986;41(2):117-20.
8. Rasool S, Siar CH, Ng KP. Oral candidal species among smokers and non-smokers. *J Coll Physicians Surg Pak.* 2005;15(11):679-82.
9. Serefko AD, Poleszak EJ, Malm A. *Candida albicans* Denture Biofilm and its Clinical Significance. *Pol J Microbiol.* 2012;61(3):161-7.
10. Gasparoto TH, Dionisio TJ, de Oliveira CE, Porto VC, Gelani V, Santos CF, et al. Isolation of *Candida dubliniensis* from denture wearers. *J Med Microbiol.* 2009;58(Pt 7):959-62.
11. Ogun HD, Bennett MH. Carcinoma of the dorsum of the tongue: a rarity or misdiagnosis. *Br J Oral Surg.* 1978;16(2):115-24.
12. Farman AG, van Wyk CW, Dreyer WP, Staz J, Thomas CJ, Louw JH, et al. Central papillary atrophy of the tongue and denture stomatitis. *J Prosthet Dent.* 1978;40(3):253-6.
13. Arendorf TM, Walker DM. Tobacco smoking and denture wearing as local aetiological factors in median rhomboid glossitis. *Int J Oral Surg.* 1984;13(5):411-5.
14. Shindo T. Median rhomboid glossitis caused by tongue-brushing. *Cleve Clin J Med.* 2023;90(1):15-6.
15. John, H. A., et al. (2023). "Median Rhomboid Glossitis: A Developmental Disorder Involving the Central Part of the Tongue." *Cureus* 15(11): e4890
16. Reamy, B. V., Derby, R. Bunt, C. W. (2010). Common tongue conditions in primary care. *Am Fam Physician, 81*(5), 627-34.