

## *Candida*-Associated Denture Stomatitis: Clinical Relevant Aspects

Andréa Araújo de Vasconcellos<sup>1\*</sup>, Amanda Araújo de Vasconcellos<sup>2</sup>, Rômulo Bomfim Chagas<sup>3</sup> and Leticia Machado Gonçalves<sup>4</sup>

<sup>1</sup>Faculty of Dentistry, Federal University of Ceará, Sobral, Ceará, Brazil

<sup>2</sup>Faculty of Medicine, Federal University of Ceará, Fortaleza, Ceará, Brazil

<sup>3</sup>Faculty of Dentistry, Federal University of Ceará, Fortaleza, Ceará, Brazil

<sup>4</sup>Ceuma University, UNICEUMA, São Luis, Maranhão, Brazil

\*Corresponding author: Andréa Araújo de Vasconcellos, Federal University of Ceará, Sobral, Ceará, Brazil, Tel: +55 85 81837676; Fax: +55 88 36132603; E-mail: andrea.odonto@yahoo.com.br

Rec date: Jun 06, 2014; Acc date: Jul 14, 2014; Pub date: Jul 20, 2014

Copyright: © 2014 Vasconcellos AA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### Abstract

*Candida*-associated denture stomatitis is a common fungal infection that affects removable denture wearers. Although *Candida spp* are considered commensal fungal in the oral cavity, changes in local and/or systemic predisposing factors related to the host conditions may lead to pathogenic form and cause disease. The clinical manifestations are usually associated with the predisposing factors, changing from no symptoms to severe pain and difficulty swallowing. The therapeutic strategies commonly adopted in the clinical practice are the use of topical and/or systemic antifungal, in addition to removing mechanically the plaque from denture surfaces and from underlying mucosa and giving instructions about the correct oral hygiene to the patient. In this context, considering the high prevalence of this disease, a review about the etiology, risk factors, clinical manifestations and therapy management of these patients is of utmost importance.

**Keywords:** *Candida*; Risk factors; Denture stomatitis; Therapeutics

### Introduction

*Candida*-associated denture stomatitis is a predominantly fungal infection that affects the human oral cavity [1]. Although *Candida spp* may be involved during infection, *Candida albicans* are considered the main pathogens, and have been found in a commensalism form in the oral cavities of adults and children, without any clinical disease [2]. These microorganisms are encountered in the dentition, tongue, cheeks, palatal mucosa, restorative materials and oral prostheses [3].

However, local and/or systemic predisposition factors may lead commensal microorganisms to pathogenic form, providing an oral environment adequate to the adhesion of microorganisms to the denture surface and mucosal epithelial cells [4]. This is followed by cell multiplication, organization and secretion of extracellular matrix, resulting in the formation of biofilm, a three-dimensional structure extremely organized [5].

Also, *C. albicans* may be found in two major forms, yeast and hyphae form. The yeast form is usually associated with mucosal commensalism, although the conversion yeast-to-hyphae is commonly related to the invasion of superficial layers of the oral epithelium, leading to clinical infection [6].

### Epidemiology

Although *C. albicans* have been the main pathogens of *Candida* - associated denture stomatitis (CADS), *Candida glabrata*, *Candida tropicalis* and *Candida parapsilosis* have been found less frequently [7,8]. Some factors favor the development of *C. albicans* biofilms, such as its capability to stick and proliferate through the denture surfaces and oral mucosal epithelial and produce a complex and heterogeneous bacterial biofilm [9].

CADS has been found in 60-65% of the denture wearers with more diffused clinical manifestations, but considering the patients that do not manifest clinical signs of inflammation and infection, this percentage increases to 75% [9,10]. It was reported that CADS is the most common oral mucosal lesion associated with removable dentures [11], and affects one in every three complete denture wearers [12].

### Risk factors

The changes from commensal to pathogenic form of *Candida spp* are typically caused by local and/or systemic predisposing factors related to the host conditions, favoring the development of the disease. While the local factors provide an adequate oral environment to biofilm development, the systemic factors influence the defense host mechanisms [2,9].

### Local factors

The local factors are important to favor the biofilm accumulation in the oral environment. In this context, different factors such as irradiation, trauma, xerostomy, complete denture wearers, poor dental hygiene, smoking, carbohydrate-rich diet and environmental pH will be discussed.

The irradiation is considered a risk factor, considering that leads to hyposalivation [13]. Also, xerostomy is another condition that reflects the decrease or the complete absence of saliva [14], reducing the ability of cleaning and buffering of saliva. Furthermore, previous study showed that patients with xerostomy induce changes that reflect in the normal microbial communities, favoring the proliferation of bacteria as *Staphylococcus aureus*, that inhibits the normal adaptation of the commensal fungal [10].

Cigarette smoke may favor CADS, considering the changes that cause in the oral cavity, influencing on saliva, oral commensal bacteria

and fungi, especially *Candida*, the main fungal related to CADs [15]. Another important factor is trauma. Although trauma alone does not induce to generalize CADs, it should be considered that trauma acts as a co-factor, favoring the adhesion and penetration of the yeasts in the oral epithelium mucosa of the host [16]. Denture trauma due to poorly adapted denture is an important co-factor of CADs.

Complete denture wearers are also a risk factor, considering that *Candida spp* are frequently found on oral mucosa and on denture surfaces [3,17]. In addition, it was observed that the presence of *C. albicans* in the oral cavity in patients with dentures was higher than in patients who do not use dentures [17]. Furthermore, poor oral hygiene favors the biofilm development [18], and it is important to have correct oral hygiene instructions.

A carbohydrate-rich diet also favors the microorganisms' adhesion and proliferation, taking into account that the carbohydrates are the primary and preferred nutrient source for *Candida spp* [19], and may modulate biofilm development on denture surface by affecting both structural features and virulence factor in *C. albicans* biofilms [20].

Finally, the environmental pH may act as a potential inducer of biofilm development [21], and previous study showed that acidic pH (pH 5.5) may be more favorable for biofilm formation [22].

### Systemic factors

There are a lot of systemic conditions that may influence the development of CADs. Here, it will be emphasized the diabetes, chemotherapy, hemophilia and immunosuppressed patients.

Diabetes mellitus is one of the chronic systemic factors with major influence of the oral environment [23]. Considering the lower glycemic control, the high glucose level on oral fluid and the immune dysregulation, the diabetes frequently causes xerostomy, which favors fungal proliferation [24].

Furthermore, patients undergoing chemotherapy are particularly affected by CADs, due to high sensibility of the oral tissues to the toxic effects of chemotherapy. Antineoplastic drugs act on proliferating cells without distinguishing the normal cells from cancerous cells. In this context, the constant cell renewal of the oral mucosa, the complex microbiota (greatly altered with the use of anticancer drugs), xerostomy, neutropenia and immunosuppression resulted from the treatment facilitate proliferation of *Candida spp* in the oral environment [25].

Hemophilia is another important risk factor for CADs. A previous study showed that 64% of hemophiliacs' patients had pre-existing infections or reduction in salivary flow [26]. Finally, the major risk factor for the proliferation of *C. albicans* is immunosuppression, which changes the homeostasis of human host. It was revealed that 87.5% of the HIV-positive patients were *Candida* positive in saliva [26].

### Clinical manifestations

There are several forms of oral candidiasis, such as Pseudomembranous Candidiasis, Erythematous Candidiasis, Angular Cheilitis and Chronic Hyperplastic Candidiasis. Here we will emphasize the CADs, a type of erythematous candidiasis that occurs under a removable denture.

Clinical characteristics may range from no symptoms to severe pain and difficulty swallowing [2,27]. The most common signs include

changes in color and texture of the mucosa, dry mouth, painful symptomatology and erythematous aspect [28].

Newton (1962) proposed a classification of the disease based on clinical aspects of the lesions: punctiform hyperemia (class I), diffuse hyperemia (class II) and granular hyperemia (class III) [29].

Punctiform hyperemia (Class I): hyperemia signs of the minor palatine salivary glands; there is an erythematous punctiform aspect, and small or diffuse areas in palate may be affected.

Diffuse hyperemia (Class II): smooth and atrophic mucosa, with erythematous aspect under the denture. It is considered the most common aspect of CADs.

Granular hyperemia (Class III): more common in dentures with suction chambers. Affect the central region of the palate, with rough and nodular appearance of the mucosa.

It is important to highlight that the therapeutic test is a widely used diagnostic measure, which consists of prescribing topical antifungals and evaluate if there is a regression of signs and symptoms of the disease, to observe if the clinical manifestations are related to CADs. When there is a regression of the lesion after the treatment, ranging from 7 to 14 days, it may be assumed that the clinical manifestations were associated with CADs [30].

### Therapy strategies

The treatment of CADs consists in removing the etiological agent, give instructions for the patient in relation to oral hygiene of denture surface and oral mucosa and treat the affected tissue. In addition, the professional should evaluate the necessity to construct another denture, considering that infected prosthetic devices typically must be removed [31].

While the patient uses the denture, the miconazole 2% has been successfully used, being commercially available in form of gel, and can be applied directly in the denture surface previously cleaned. It should be used 2 to 3 times a day for one or two weeks, according the patient response [30]. In addition, a topical antifungal agent widely used for the treatment of CADs is nystatin, which can be used on the oral mucosa several times a day, being available as a liquid suspension, cream and pastille [2].

When the therapy via topical antifungal agents does not lead to clinical improvement of the patient, the use of systemic antifungal agents is recommended, especially in immunosuppression patients. The fluconazole (FLZ) has been extensively used, taking into account that has lower toxicity, it is highly bioavailable in oral formulations, and less expensive in relation to other antifungal agents [32]. It is recommended a single and daily dose, being the first dose of 400 mg and subsequent daily doses of 100 mg for one or two weeks [33]. Another systemic antifungal agent is ketoconazole, which is absorbed from the gastrointestinal tract and must be administered in a single dose of 200 mg during 14 days. This is a hepatotoxic drug and can cause cardiac arrhythmias when used in combination with antihistamines or macrolide antibiotics [34,35]. For a long time, amphotericin B was used in the treatment of CADs. However, it is extremely nephrotoxic and is administered intravenously, being nowadays less used in CADs therapy.

## Conclusion

The knowledge about *Candida* -associated denture stomatitis is of utmost importance in clinical practice. The professional should recognize the possible risk factors for CADS and the clinical manifestations, in order to indicate the correct treatment for the patients.

## References

1. Harriott MM, Noverr MC (2011) Importance of Candida-bacterial polymicrobial biofilms in disease. Trends Microbiol 19: 557-563.
2. Lalla RV, Patton LL, Dongari-Bagtzoglou A (2013) Oral candidiasis: pathogenesis, clinical presentation, diagnosis and treatment strategies. J Calif Dent Assoc 41: 263-268.
3. Sánchez-Vargas LO, Estrada-Barraza D, Pozos-Guillen AJ, Rivas-Caceres R (2013) Biofilm formation by oral clinical isolates of Candida species. Arch Oral Biol 58: 1318-1326.
4. Sardi JC, Scorzoni L, Bernardi T, Fusco-Almeida AM, Mendes Giannini MJ (2013) Candida species: current epidemiology, pathogenicity, biofilm formation, natural antifungal products and new therapeutic options. J Med Microbiol 62: 10-24.
5. Jayatilake JA (2011) A review of the ultrastructural features of superficial candidiasis. Mycopathologia 171: 235-250.
6. Vallejo JA, Sánchez-Pérez A, Martínez JP, Villa TG (2013) Cell aggregations in yeasts and their applications. Appl Microbiol Biotechnol 97: 2305-2318.
7. Vazquez JA, Sobel JD (2002) Mucosal candidiasis. Infect Dis Clin North Am 16: 793-820, v.
8. Dorocka-Bobkowska B, Konopka K (2007) Susceptibility of candida isolates from denture-related stomatitis to antifungal agents in vitro. Int J Prosthodont 20: 504-506.
9. Salerno C, Pascale M, Contaldo M, Esposito V, Busciolano M, et al. (2011) Candida-associated denture stomatitis. Med Oral Patol Oral Cir Bucal 16: e139-143.
10. Webb BC, Thomas CJ, Willcox MD, Harty DW, Knox KW (1998) Candida-associated denture stomatitis. Aetiology and management: a review. Part 2. Oral diseases caused by Candida species. Aust Dent J 43: 160-166.
11. Cueto A, Martínez R, Niklander S, Deichler J, Barraza A, et al. (2013) Prevalence of oral mucosal lesions in an elderly population in the city of Valparaiso, Chile. Gerodontology 30: 201-206.
12. Zissis A, Yannikakis S, Harrison A (2006) Comparison of denture stomatitis prevalence in 2 population groups. Int J Prosthodont 19: 621-625.
13. Nett JE, Marchillo K, Spiegel CA, Andes DR (2010) Development and validation of an in vivo Candida albicans biofilm denture model. Infect Immun 78: 3650-3659.
14. Webb BC, Thomas CJ, Willcox MD, Harty DW, Knox KW (1998) Candida-associated denture stomatitis. Aetiology and management: a review. Part 1. Factors influencing distribution of Candida species in the oral cavity. Aust Dent J 43: 45-50.
15. Soysa NS, Ellepola AN (2005) The impact of cigarette/tobacco smoking on oral candidosis: an overview. Oral Dis 11: 268-273.
16. Emami E, de Grandmont P, Rompré PH, Barbeau J, Pan S, et al. (2008) Favoring trauma as an etiological factor in denture stomatitis. J Dent Res 87: 440-444.
17. Emami E, de Grandmont P, Rompré PH, Barbeau J, Pan S, et al. (2008) Favoring trauma as an etiological factor in denture stomatitis. J Dent Res 87: 440-444.
18. Daniluk T, Tokajuk G, Stokowska W, Fiedoruk K, Sciepek M, et al. (2006) Occurrence rate of oral Candida albicans in denture wearer patients. Adv Med Sci 51 Suppl 1: 77-80.
19. Emami E, Kabawat M, Rompre PH, Feine JS (2014) Linking evidence to treatment for denture stomatitis: a meta-analysis of randomized controlled trials. J Dent 42: 99-106.
20. Ene IV, Adya AK, Wehmeier S, Brand AC, MacCallum DM, et al. (2012) Host carbon sources modulate cell wall architecture, drug resistance and virulence in a fungal pathogen. Cell Microbiol 14: 1319-1335.
21. Santana IL, Gonçalves LM, de Vasconcellos AA, da Silva WJ, Cury JA, et al. (2013) Dietary carbohydrates modulate Candida albicans biofilm development on the denture surface. PLoS One 8: e64645.
22. Davis D (2003) Adaptation to environmental pH in Candida albicans and its relation to pathogenesis. Curr Genet 44: 1-7.
23. Vasconcellos AA, Gonçalves LM, Del Bel Cury AA, da Silva WJ (2014) Environmental pH influences Candida albicans biofilms regarding its structure, virulence and susceptibility to fluconazole. Microb Pathog 69-70: 39-44.
24. Girtan M, Zurac S, Stăfncianu F, Bastian A, Popp C, et al. (2009) Oral epithelial hyperplasia in diabetes mellitus. Rom J Intern Med 47: 201-203.
25. Lotfi-Kamran MH, Jafari AA, Falah-Tafti A, Tavakoli E, Falahzadeh MH (2009) Candida Colonization on the Denture of Diabetic and Non-diabetic Patients. Dent Res J (Isfahan) 6: 23-27.
26. Wilberg P, Hjermsstad MJ, Ottesen S, Herlofson BB (2014) Chemotherapy-Associated Oral Sequelae in Patients With Cancers Outside the Head and Neck Region. J Pain Symptom Manage .
27. Pereira CM, Pires FR, Corrêa ME, di Hipólito Júnior O, Almeida OP (2004) Candida in saliva of Brazilian hemophilic patients. J Appl Oral Sci 12: 301-306.
28. Wilson J (1998) The aetiology, diagnosis and management of denture stomatitis. Br Dent J 185: 380-384.
29. de Oliveira CE, Gasparoto TH, Dionísio TJ, Porto VC, Vieira NA, et al. (2010) Candida albicans and denture stomatitis: evaluation of its presence in the lesion, prosthesis, and blood. Int J Prosthodont 23: 158-159.
30. Newton AV (1962) Denture sore mouth: a possible etiology. Br Dent J 1: 357-360.
31. Williams DW, Lewis MA (2000) Isolation and identification of Candida from the oral cavity. Oral Dis 6: 3-11.
32. Montejo M (2011) Epidemiology of invasive fungal infection in solid organ transplant. Rev Iberoam Micol 28: 120-123.
33. Spellberg BJ, Filler SG, Edwards JE Jr (2006) Current treatment strategies for disseminated candidiasis. Clin Infect Dis 42: 244-251.
34. Ramage G, VandeWalle K, Bachmann SP, Wickes BL, López-Ribot JL (2002) In vitro pharmacodynamic properties of three antifungal agents against preformed Candida albicans biofilms determined by time-kill studies. Antimicrob Agents Chemother 46: 3634-3636.
35. Redding S, Bhatt B, Rawls HR, Siegel G, Scott K, et al. (2009) Inhibition of Candida albicans biofilm formation on denture material. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 107: 669-672.