



Original Research Article

Relation between candidiasis and linear gingival erythema in HIV-positive patients

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Abstract

Objective: To assess the prevalence of candidiasis associated with Linear Gingival Erythema (LGE) in patients with HIV. Material and methods: Patients with HIV who sought care were identified and those with linear gingival erythema were included in the study. Initially, a questionnaire divided into two parts was applied, the first session consisting of personal and sociodemographic data and the second session containing questions related to health habits. Then, erythema samples were collected with a collector brush and cultivated in petri dishes containing CHROMagar for 3 days under aerobic conditions at room temperature. Plaque evaluation and colony counts were performed. **Results:** From a total of 46 patients, thirteen were included in the study. Among the samples, eleven were diagnosed with C. albicans and five were diagnosed with other species of Candida sp. Conclusion: A high prevalence of Candida sp. was observed on patients with lesions of linear gingival erythema and diagnosed with HIV.

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Introduction

Linear gingival erythema (LGE) is a lesion defined as an intense reddish line, most commonly found in anterior teeth, involving the free marginal gingiva and could be extended to the inserted gingiva. It may be symptomatic and in some cases accompanied by bleeding on probing and discomfort. This condition usually manifests itself in immunosuppressed individuals [10, 15]. LGE is known as a non-biofilm-induced lesion, since the amount of biofilm present is often disproportionate [3, 9, 13], as well as not responding to conventional periodontal therapy, including plaque control, scaling and root planning [14, 16]. It was observed that in HIV-positive individuals with LGE there are a high number of neutrophils in the gingival epithelium. These phagocytes invade the entire gingival epithelium, which may cause possible tissue ulcerations [6].

Some facts have not been completely elucidated yet in relation to LGE, such as whether this condition can progress to more severe forms of periodontal disease. Authors also mention the possibility of LGE being a precursor of necrotizing ulcerative periodontitis in HIV-infected patients [7, 10, 14, 16], emphasizing the importance of identifying LGE in HIV-infected patients and the need for further studies on this condition [16].

A possible relation between the two clinical manifestations reported, linear gingival erythema and candidiasis was cited and discussed in the literature by different authors [7, 8, 6]. Grbic et al. [8] observed an intimate association between subgingival colonies of Candida species in lesions of linear gingival erythema in HIV-positive patients [8, 10, 14]. In a histopathological study, an increase in polymorphonuclear leukocytes was found in LGE lesions in HIV-infected patients, which have activity in the control of Candida sp. infection after the invasion of tissues by these microorganisms in immunocompromised patients [6, 7]. In addition, the development of LGE was also associated with a subgingival colonization of Candida species, which seems to involve an invasion of the gingival tissue by this microorganism, a fact that could indicate and justify a possible fungal origin of the disease [6, 8]. The importance of this relationship is in the treatment of LGE, since the presence of Candida sp. within the gingival tissues may explain the inability of conventional periodontal

therapy to control linear gingival erythema [16]. Thus, the aim of this study was to evaluate the prevalence of candidiasis associated with LGE in patients with HIV.

Materials and methods

The research was performed with patients undergoing treatment at Oswaldo Cruz Hospital in Curitiba, Paraná. All the new HIV-positive patients who sought care at the evaluation days were examined and patients who presented linear gingival erythema were included in the study. The sample was for convenience.

Ethics statement

The study was approved by the Research Ethics Committee of UFPR. All participants were informed about the nature, potential risks and benefits of their participation in the study, and signed a Consent Term and receive a copy.

Inclusion criteria

Individuals with HIV infection and exhibiting LGE were included in this study.

Exclusion criteria

Individuals who took systemic antibiotics and local and systemic antifungal drugs in the last six months were excluded from the study, since the use of these medications may affect the oral microbiota independently of the presence or absence of the linear gingival erythema lesion.

A questionnaire divided into two sessions was applied to all participants. The first session comprised questions of personal data and sociodemographic data (age, gender, educational level, marital status). The second part, health habits related issues (dental hygiene, smoking and alcohol consumption). After the questionnaires were applied, clinical evaluations and biofilm collection were performed for microbiological evaluation.

After the clinical evaluation, a collection brush was passed three times over the linear gingival erythema lesion, and immediately transferred to Petri dish containing CHROMagar selective culture medium for *Candida* sp. (Laborclin) (figure 1 – A and B).



Figure 1 – A: Collection brush; B: Petri dish containing selective CHROMagar culture medium for *Candida* sp.

To transfer to content of the sample the brush was passed over the agar, as a conventional culture sample.

The CHROMagar culture medium allows the isolation of fungi and the chromogenic substrates that are included in the agar makes colonies of Candida albicans, Candida tropicalis and Candida krusei produce different colors, thus allowing a direct detection of these species of yeasts [2, 12]. The colonies of C. albicans appear light green to medium green, C. tropicalis appear greenish blue to metallic blue, and C. krusei appear light pink with a whitish border. Other yeast species may develop their natural color (cream color) or appear pink or light mauve to dark [for example, Candida (Torulopsis) glabrata and other species]. An additional advantage of this medium is the easy detection of mixed cultures of yeasts due to the presentation of their colonies with different colors [1].

The samples were cultivated and the colonies counted in the Laboratory of Basic Studies in Dentistry of the Federal University of Parana. During cultivation, the plates were stored in aerobiose and at room temperature for 3 days until colonies counting. The count of the colonies of each agar plate was made in triplicate by two evaluators, in adequate light. When there was disagreement among the examiners, an arithmetic mean was used. The number of colonies was computed per participant.

The presence of *Candida* sp. and the variables of interest, including linear gingival erythema presence, age, caries, gingival alteration and the presence of other lesions, were evaluated descriptively.

Results

A total of 46 patients were evaluated and 13 patients were included in the study according to the inclusion criteria proposed by the research project, presenting lesions and LGE (figure 2).



Figure 2 - Lesion of linear gingival erythema (LGE) in one of the evaluated patients

Thirteen patients enrolled in the study signed the free and informed consent term and answered the questionnaire with personal data and sociodemographic data (age, gender, educational level, marital status) and issues related to health habits (dental hygiene, smoking and alcohol consumption). And then, clinical examination and material collection for microbiological evaluation were performed.

Questionnaires and clinical examination

The mean age of the patients examined was 39 years (21-58). Eight patients were female and five were male. Regarding marital status and employment, there was an equivalence between single and married and between employed and non-employed patients. Regarding schooling, although there were different answers, the majority, about eight of them, reported having only attended elementary school. Only six of the patients declared themselves employed at the time of admission.

Regarding health habits, patients were questioned about the use of alcohol, cigarettes and

other drugs. Of the thirteen patients, only three affirmed at least one of the questioned habits. The results of health habits and oral condition are listed in table I. The oral condition, classified according to the findings of the clinical examination, in table II, ranged from regular to poor, in the majority of cases, of which thirteen patients had one of these conditions.

Table I - Systemic habits and oral condition evaluated per patient

Patient	Alcohol	Cigarettes	Other drugs	Oral condition
1	0	0	0	1
2	0	1	0	0
3	0	0	1	0
4	0	0	0	1
5	0	0	0	1
6	0	1	1	1
7	0	0	0	1
8	1	0	0	0
9	0	0	0	0
10*				2
11	0	0	0	1
12	0	0	0	0
13	0	0	0	0

^{***} Patient with mental weakness, and it is not possible to perform a questionnaire on health habits. For alcohol consumption, cigarettes and other drugs was considered presence or absence (1/0) and for oral condition was considered poor (0), regular (1) or satisfying (2)

During the clinical examination caries lesions, periodontal disease, absence of teeth and savory tongue were the most frequent situations.

Table II - Findings of clinical examination per patient

Patient	Caries lesions	Abscence of teeth	Periodontal disease	Biofilm	Residual root	Prostheses	Savory tongue	EGL
1	0	1	1	0	0	0	1	1
2	1	0	1	1	1	0	1	1
3	1	1	1	0	1	0	1	1
4	0	1	0	1	0	1	1	1
5	0	1	1	0	0	0	0	1
6	1	1	0	0	0	0	1	1
7	1	0	1	0	0	0	0	1
8	0	1	1	0	0	0	1	1
9	1	1	1	1	1	0	0	1
10	0	0	0	0	0	0	1	1
11	1	1	1	0	1	1	1	1
12	1	1	1	1	0	0	1	1
13	0	0	1	1	0	0	1	1

EGL: linear gingival erythema; presence: 1; absence: 0

Sample culture

Counts of UFC (Colony Unity Form) was performed after three days of growth and the results are at table III and figure 3.



Figure 3 - Sample of Candida sp. colonies from one of the patients, after three days of culture at room temperature

The colonies were classified according to the color and the presence or not of halo around the same.

- Light green and medium green colonies in the table (#): Candida albicans.
- Blue-green or metallic colonies in the table (##): Candida tropicalis.
- Colonies with pink and whitish halo, in the table (*): Candida krusei.
- Creamy colonies, light or dark mauve and pink, represented in table as (**): other species.

C. albicans was the most present specie. Eleven patients out of thirteen were diagnostic with this specie. The counts of UFC cultivated from patients samples were from seven to 582. Five patients were diagnostic with other species of *Candida* sp. (table III).

Table III - Count of colonies and Candida species found in the culture medium, per patient

NUMBER OF COLONIES							
Patients	Candida species found						
	C. albicans#	C. tropicalis##	C. krusei*	Others species**			
1	8	0	0	0			
2	60	0	0	8			
3	383	0	0	0			
4	89	0	0	0			
5	185	0	0	3			
6	195	0	0	0			
7	49	0	0	0			
8	582	0	0	21			
9	11	0	0	3			
10	0	0	0	0			
11	121	0	0	9			
12	0	0	0	0			
13	7	0	0	0			

Discussion

The diagnosis of LGE was performed in 28% of the evaluated population. Of these patients (n=13), 85% also had the presence of *Candida* sp. These data corroborate with the literature, which has been discussing the possible relationship between linear gingival erythema and candidiasis [6-8]. Among the Candida species cultured from the samples collected, the most prevalent was *Candida albicans*, which is also the most commonly found in HIV-positive patients [4].

In the present study nine patients (69%) presented periodontal disease associated with LGE and *Candida* sp. The high risk for aggressive periodontal diseases has also been reported for patients with the AIDS virus [11]. However, chronic periodontitis has not yet been published in the literature on increased risk, especially for patients receiving antiretroviral therapy [7].

Although detailed periodontal exams have not been performed, 69% is a high prevalence. Moreover, patients presented dental cavities, residual roots, that is, a well-compromised oral health, which may be related to that demonstrated by Ferreira *et al.* [5], who observed that the periodontal microbiota of HIV + patients is more diverse and complex than that of non-virus positive patients, and therefore the association with Candida fungus may also be part of this high diversity.

Although data from this study have demonstrated the high prevalence of candidiasis in patients with linear gingival erythema, one cannot extrapolate this relation to a causal relation, since the present study only observed the presence and frequency of these associated lesions in a small group of patients. However, it is a guide for future studies that may be directed to: 1) compare the prevalence of *Candida* sp. in HIV-positive patients who do not have linear gingival erythema beyond the evaluation of treatments, mainly to be able to compare the evolution of linear gingival erythema with or without treatment directed to Candidiasis.

Conclusion

A high prevalence of *Candida* sp. was observed in patients with linear gingival erythema lesions and diagnosed with HIV, with approximately 85% of subjects testing positive for *C. albicans*.

References

- 1. Balows A. Book review: Manual of clinical microbiology 8th edition: P. R. Murray, E. J. Baron, J. H. Jorgenson, M. A. Pfaller, and R. H. Yolken, eds., ASM Press, 2003, 2113 pages, 2 vol, 2003 + subject & author indices, ISBN: 1-555810255-4, US\$ 189.95. Diagn Microbiol Infect Dis. 2003;47(4): 625-6.
- 2. Beighton D, Ludford R, Clark DT, Brailsford SR, Pankhurst CL, Tinsley GF et al. Use of CHROMagar Candida medium for isolation of yeasts from dental samples. J Clin Microbiol. 1995;33(11):3025-7.
- 3. Coogan MM, Greenspan J, Challacombe SJ. Oral lesions in infection with human immunodeficiency virus. Bull World Health Organ. 2005;83(9):700-6.
- 4. Dupont B, Graybill JR, Armstrong D, Laroche R, Touzé JE, Wheat LJ. Fungal infections in AIDS patients. J Med Vet Mycol. 1992;30 Suppl 1:19-28.
- 5. Ferreira DC, Gonçalves LS, Siqueira JF Jr, Carmo FL, Santos HF, Feres M et al. Subgingival bacterial community profiles in HIV-infected Brazilian adults with chronic periodontitis. J Periodontal Res. 2016;51(1):95-102.
- 6. Gomez RS, Costa JE, Loyola AM, Araújo NS, de Araújo VC. Immunohistochemical study of linear gingival erythema from HIV-positive patients. J Periodontal Res. 1995;30(5):355-9.
- 7. Gonçalves LS, Gonçalves BM, Fontes TV. Periodontal disease in HIV-infected adults in the HAART era: clinical, immunological, and microbiological aspects. Arch Oral Biol. 2013;58(10):1385-96.
- 8. Grbic JT, Mitchell-Lewis DA, Fine JB, Phelan JA, Bucklan RS, Zambon JJ et al. The relationship of candidiasis to linear gingival erythema in HIV-infected homosexual men and parenteral drug users. J Periodontol. 1995;66(1):30-7.
- 9. Holmstrup P, Glick M. Treatment of periodontal disease in the immunodeficient patient. Periodontol 2000. 2002;28:190-205.
- 10. Maloth S, Shrinivas TR, Krishna Pramod B, Nagarathna PJ. Prevalence of oromucosal lesions in HIV positive patients receiving haart a prospective clinical study. J Family Med Prim Care. 2020;9(9):4821-5.

- 11. McKaig RG, Patton LL, Thomas JC, Strauss RP, Slade GD, Beck JD. Factors associated with periodontitis in an HIV-infected southeast USA study. Oral Dis. 2000;6(3):158-65.
- 12. Odds FC, Bernaerts R. CHROMagar Candida, a new differential isolation medium for presumptive identification of clinically important Candida species. J Clin Microbiol. 1994;32(8):1923-9.
- 13. Patton LL, Phelan JA, Ramos-Gomez FJ, Nittayananta W, Shiboski CH, Mbuguye TL. Prevalence and classification of HIV-associated oral lesions. Oral Dis. 2002;8 Suppl 2:98-109.
- 14. Peacock ME, Arce RM, Cutler CW. Periodontal and other oral manifestations of immunodeficiency diseases. Oral Dis. 2017;23(7):866-88.
- 15. Winkler JR, Murray PA. Periodontal disease. A potential intraoral expression of AIDS may be rapidly progressive periodontitis. CDA J. 1987;15(1):20-4.
- 16. Yin MT, Dobkin JF, Grbic JT. Epidemiology, pathogenesis, and management of human immunodeficiency virus infection in patients with periodontal disease. Periodontol 2000. 2007;44: 55-81.