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CANDIDA SPP. IN LINEAR GINGIVAL ERYTHEMA LESIONS IN HIV- INFECTED CHILDREN: REPORTS OF SIX CASES

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ABSTRACT

Linear gingival erythema (LGE), formally referred as HIV-gingivitis, is the most common form of HIV-associated periodontal disease in HIV-infection. These lesions were recently evaluated as a possible form of erythematous oral candidosis, mainly caused by *Candida albicans*. Other species are also being associated such as *C. tropicalis*, *C. stellatoidea*, *C. krusei*, *C. parapsilosis*, *C. glabrata* and *C. dubliniensis*, that was identified in some HIV-infected subjects. This case report demonstrates the presence of typical LGE lesions in six HIV-infected children, also investigates the etiologic agent by microbiological exams and correlates this oral manifestation with patients' systemic conditions. Microbiological analyses showed positive growth for *Candida* spp in all patients, all of whom had severe imunessupression. After antifungal medication, the regression of lesions could be note. The presence of LGE in pediatric patients with AIDS may indicate its feature as a predictive marker in progression of HIV-infection in children.

INTRODUCTION

Oral candidiasis (OC) is the most common opportunistic infection seen in HIV-infected children (RAMOS-GOMEZ, 1999; PORTELA ET AL., 2000; SANTOS ET AL., 2001) and it is presented as pseudomembranous and erythematous candidiasis, and angular cheilitis.

Linear gingival erythema (LGE), which was formally referred as HIV-gingivitis, is the most common form of HIV-associated periodontal disease in HIV-infected population. It is considered resistant to conventional plaque-removal therapies, being considered, nowadays, a lesion of fungal etiology (RAMOS-GOMEZ, 1999; LAMSTER ET AL., 1998; HOLMSTRUP & WESTERGAARD, 2000). It is characterized by a fired, linear band 2 to 3 mm wide on the marginal gingival accompanied by petechiae-like or diffuse red lesions on the attached gingival and oral mucosa, and may be accompanied by bleeding. The prevalence of this lesion varies widely in different studies, ranging from 0 to 48% (RAMOS-GOMEZ, 1999; PORTELA ET AL., 2000; SANTOS ET AL., 2001; CASTRO, SOUZA & FONSECA, 1999; CASTRO ET AL., 2000), probably because in many of them, LGE was misdiagnosed as gingivitis.

Mucosal candidiasis is an infection of fungal etiology mainly caused by *Candida albicans* (RAMOS-GOMEZ, 1999), although other species are being associated such as *C. tropicalis*, e *C. stellatoidea*, *C. krusei*, *C. parapsilosis*, e *C. glabrata* (BAUMGARTNER, FREYDIERE & GILLE, 1996). Also, *C dubliniensis*, was identified in HIV-infected subjects and following studies (MEILLER ET AL., 1999; BROWN ET AL., 2000) demonstrated the presence of this yeast in positive cultures for *C. albicans* in HIV-infected children who had severe immunossuppression.

Velegraki et al. (1999) presented case reports in which there was a strong evidence that linear gingival erythema was of candidal origin. Those lesions were clinically evaluated as a possible form of erythematous oral candidosis. Microbiological exams (direct microscopic examination, culture, biochemical and serological tests) identified *C .albicans* in three pediatric patients and *C. dubliniensis* in one patient. In addition, all lesions healed on antimycotic treatment.

Therefore, the objective of this article is to report the presence of linear gingival erythema lesions in six HIV-infected children, investigate the etiologic agent, and correrelate this oral manifestation with patients' systemic conditions.

CASE REPORT

Six vertically HIV-infected children, all patients from a Pediatric AIDS Outpatients Clinic of Universidade Federal do Rio de Janeiro - UFRJ, Rio de Janeiro, Brazil, attendend by the staff of The Dental Program for Oral Helth were diagnostic as having oral lesions during routine exams.

All children had definitive diagnosis for HIV infection confirmed by 2 positive ELISA tests and 1 positive Western Blot. The examinations were performed by a single trained pediatric dentist, after, supervised toothbrushing with fluoridated toothpaste, followed by topical fluoride application (2.0 % sodium fluoride).

Intraoral exam revealed the presence of a linear gingival erythema and the lesions from all children were resistant to conventional plaque-removal therapy (Figure 1).

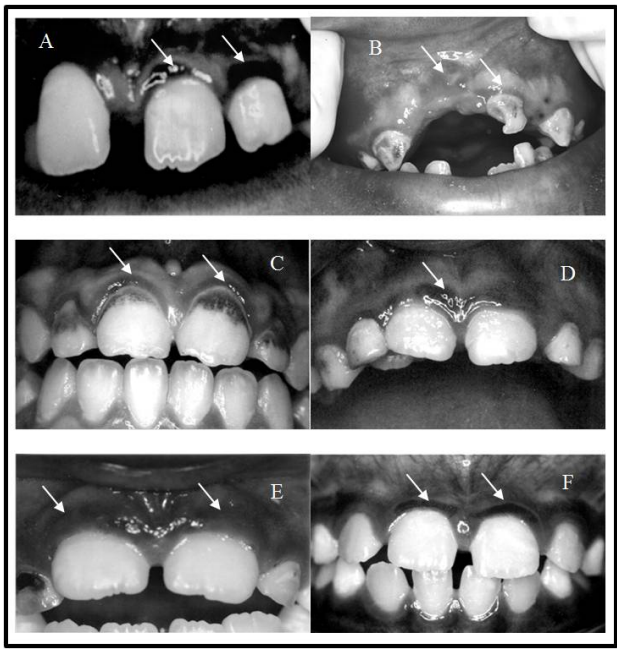

Figure 1: Clinical aspects of the oral lesions : A – patient 1; B – patient 2; C – patient 3; D – patient 4; E – patient 5; F – patient 6.

Other oral manifestations found in all patients were bilateral submandibular gland enlargement. Patient 1 presented pseudomembranous candidiasis in the jugal mucosa and dorsum of the tongue, while patient 3 presented erythematous candidiasis in the hard palate mucosa.

All data regarding patient's personal information, medical history and laboratorial exams (the closest ones to sample collection) such as immunological and clinical classification (CDC classification), percentage of CD4-positive cells and viral load were collected from their medical records (Table 1).

TABLE 1: PATIENT'S MEDICAL INFORMATION AND ORAL EXAMINATION DATA

Patient	CDC Classification	Age (years) /Sex	Race	ELG Localization (buccal or lingual gingiva)	Orofacial lesions	Anti-retroviral therapy
1	C3	12/ F	Caucasian	Anterior maxillary/ mandibular and 16,26 (lingual)	Pseudomembranous candidiasis	Yes
2	C3	7/ M	Caucasian	All teeth, except the 31,41	-	Yes
3	C3	10/ M	Afro-descedent	Anterior maxillary/ mandibular	Erytematous Candidiasis	Yes
4	B3	4/ F	Caucasian	Anterior maxillary teeth (buccal)	-	Yes
5	C2	11/ F	Afro-descedent	21 (buccal)	-	Yes
6	C3	11/ M	Afro-descedent	11,21 (buccal)	-	Yes

NOTE: N- no symptoms; A- mild symptoms; B-moderate symptoms; C-severe symptoms; 1-absence of immunessupression; 2- moderate immunessupression; 3- severe immunessupression
Source: *1994 Revised classification system for Human Immunodeficiency Virus infection in children less than 13 years of age (CDC)*

MYCOLOGICAL INVESTIGATION

The samples for mycological investigation was obtained by frictionating a sterilized microbrush on the lesion (LGE) and then transferred to test tubes. They were smeared on CHROMagar Candida® plates for culture and incubated at 37ºC. This culture medium allows a presumptive identification of common clinical isolates of *Candida* through the production of different coloured colonies (ODDS & BERNAERTS, 1994). Each different coloured colony was then identified through biochemical tests of sugar assimilation and fermentation, using the API 20C (Biomerieux, Marcy L'Etoile, France). Plates with positive growth were classified according to Lamey et al (1988): mild growth (< 10 cfu/ml of saliva), moderate (11-49 cfu/ml) and strong (>50 cfu/ml). The results of quantification and identification of *Candida* spp. from LGE lesions, as well as the relation with their systemic conditions can be observed in Table2.

TABLE 2: RELATION BETWEEN PATIENTS' SYSTEMIC CONDITIONS AND THE LEVEL OF CANDIDA SPP PRESENT IN LINEAR GINGIVAL ERYTHEMA LESIONS.

Patient	Clinical Classification	Viral load	CD4 cells count (%)	Isolates of *Candida*	Growth classification
1	C3	170.000	1,0	*C. albicans*	Mild
2	C3	66.000	3,0	*C. albicans*	Strong
3	C3	110.000	12,0	*C. albicans*	Strong
				C. tropicalis	Strong
4	B3	37.000	18,5	*C. albicans*	Mild
5	C2	280.000	27,0	*C. dubliniensis*	Strong
6	C3	900	35,0	*C. albicans*	Strong

NOTE: N- no symptoms; A- mild symptoms; B-moderate symptoms; C-severe symptoms (AIDS)

1-absence of immunessupression; 2- moderate immunessupression; 3- severe immunessupression (AIDS)

Source: 1994 Revised classification system for Human Immunodeficiency Virus infection in children less than 13 years of age (CDC).

Mycological investigation, demonstrated the presence of Candida spp in all LGE lesions. The patients were referred to their clinicians in order to choose the most appropriate antifungal therapy for each child and also received oral hygiene and dietary instructions. Those with dental needs were referred to the pediatric dental clinic of the same university. After the use of topical antifungal treatment (Daktarin® oral gel - Miconazole) for 7 days it could be note the regression of all lesions. Patients were been under periodically follow up for maintenance of oral health for 8 years. During this time, patients were introduced for antiretroviral HAART therapy and were medically controlled.

DISCUSSION

In these six case reports, the fact that all patients presented typical linear gingival erythema lesions, which were resistant to conventional plaque-removal therapies, has lead to a microbiological investigation. This investigation provided strong evidence that LGE in HIV-infected children may be considered of fungal etiology, since Candida spp were isolated from all LGE lesions. These findings corroborate the study of Velegraki et al. (1999) in which HIV-pediatric patients presented LGE with positive cultures for Candida spp. (VELEGRAKI ET AL., 1999). They are also in agreement with the consulted literature which classifies LGE as a lesion of fungal etiology (RAMOS-GOMEZ, 1999; LAMSTER ET AL., 1998; HOLMSTRUP & WESTERGAARD, 2000).

Candida albicans was the most frequent species isolated, encountered in five of six patients, which confirms that such yeast is the main etiologic agent of mucosal candidiasis (RAMOS-GOMEZ, 1999). One patient presented a mixed culture of C. albicans and C. tropicallis, confirming the association of other species rather than C. albicans isolates with oral candidiasis (BAUMGARTNER, FREYDIERE & GILLE, 1996). Another patient exhibited positive growth for Candida dubliniensis indicating that this species is also present in oral pediatric HIV seropositive population (BROWN ET AL., 2000; VELEGRAKI ET AL., 1999). In 2004, Portela et al. also demonstrated, the presence of Candida dubliniensis in subgingival sites of HIV-positive children, indicating that this species has emerged as another pathogen noted for its in vitro potential for azole resistance and its enhanced in vitro adherence to human buccal epithelial cells.

Regarding patients' medical history, it could be observed that all patients with LGE had AIDS disease, according to CDC classification (CDC, 1993), presented severe clinical signs and symptoms and/or severe immunossuppression. Castro et al. (2000) studied the correlation between oral manifestations and the clinical/immunological classification of HIV-infected children, which demonstrated that patients who were severely debilitated (high viral load and low CD4 percentage) presented oral lesions such as linear gingival erythema. Similar results were also observed in HIV-seropositive adults, demonstrating a trend for more LGE lesions with lower CD4+ cells (GRBIC ET AL., 1995).

Other orofacial lesions associated to HIV-infection, as erythematous and pseudomembranous candidiasis and hairy leukoplakia, are considered markers for immunossuppression and AIDS (KATZ ET AL., 1993; GLICK ET AL., 1994; PORTELA AL., 2002). The present case also revealed that all patients who had LGE presented severe signs and symptoms of immunossuppression, which may suggest that, this lesion might be considered a prognostic indicator of HIV-infection.

The patients were referred to their clinicians, once they would be able to prescribe the most appropriate antimycotic treatment, because some antifungal may have a cross-reaction with some antiretrovirals. One example is the metabolism process for elimination of ketoconazole and AZT (zidovudine), which is dependent on cytochrome-C cellular system, unabling the concomitant prescription of both medications.

The oral examination is an essential component for early recognition of disease progression, once many oral lesions may occur as one of first clinical signs and symptoms of HIV-infection in pediatric population. The findings of this case report may suggest that the presence of linear gingival erythema lesions might be considered a marker in the progression of HIV-infection in a pediatric population. And therefore, studies should be conducted in order to evaluate the prognosis of this lesion in HIV-infected children.

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