Oral soft tissue manifestations and CD4 lymphocyte counts in HIV-infected children

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Abstract

This study investigated the prevalence of oral soft tissue lesions in children infected with HIV and the relationship of CD4 lymphocyte levels with the prevalence of those lesions. Sixty HIV-positive children enrolled in the Children's Hospital AIDS Program (age 5.8 ± 3 years) were selected for study. Only five subjects (8%) had healthy gingiva and a low mean plaque index (22%). The remainder had gingivitis or periodontitis with relatively high plaque indices (47, 55, and 94%, respectively). A declining CD4 lymphocyte count (1357 to 35) was associated with an increasing severity of gingival disease. (Pediatr Dent 18:117-20, 1996)

HIV infection in children was first described in 1983. Since then, there have been a limited number of reports of the oral manifestations associated with this disease. Several reports list oral candidiasis as the most prevalent lesion. Other oral manifestations of HIV infection in children include parotid gland enlargement, herpes simplex, and hairy leukoplakia. Only two studies have included the prevalence of gingival lesions. Likewise, there are limited data concerning oral soft tissue lesions and their relationship to CD4 lymphocyte levels. This study investigated the prevalence of soft tissue and gingival lesions in 60 HIV-infected pediatric patients and the relationship of CD4 lymphocyte levels with the prevalence of selected common oral lesions.

Methods and materials

Sixty HIV-infected children in the Children's Hospital AIDS Program (CHAP) who were consecutively enrolled in 1990 received a comprehensive oral examination. All of the children were confirmed to be HIV+ by positive ELISA (HIV), confirmed by Western Blot, and met the Centers for Disease Control and Prevention (CDC) diagnostic criteria of Class P-2 infection. The mean age of those examined was 5.8 ± 3 years with a range of 1 to 18 years. The sample consisted of mostly African Americans (62%, 37/60), followed by equal numbers of Caucasians (17%, 10/60) and Hispanics (18%, 11/60). The remaining children were Asian (2/60) or Haitian (2/60). Males accounted for 43% (N = 26), and females accounted for 57% (n = 34). Fifty-five of the 60 patients had contracted the disease perinatally, three were infected by blood transfusion, and two had been sexually abused. All children had acquired the infection prior to 13 years of age.

Oral examinations

Informed consent was obtained from the patients' parents or guardians and oral examinations were performed at the CHAP independently by two investigators (RBH, JJJ). The two sets of examinations were then compared to establish inter-rater reliability of 96%. Soft tissue lesions were diagnosed using criteria suggested at the time that this study was conducted. Other oral manifestations were diagnosed by clinical findings. Pseudomembranous and erythematous candidiasis were grouped together with angular cheilitis. Herpes simplex was diagnosed by clustered vesicles or multiple, painful intra-oral ulcers and a clinical response to Acyclovir® (Burroughs Wellcome / Glaxo Wellcome Inc, Research Triangle Park, NC).

A simplified gingival index (modified from the index developed by Loe and Silness) was performed with a 0-3 scale. The gingiva examined was divided into four scoring units: distofacial papilla, facial, mesiofacial papilla, and the lingual margin. The maxillary central and lateral incisors (primary or permanent) were the only areas examined, to ensure consistency of teeth available for examination. A composite score was obtained by averaging the individual scores for the gingiva around each tooth sampled to give an overall gingival index (0-3) for the entire segment.

A plaque index of the maxillary central and lateral incisors was also performed. This was a version of the Modified Plaque Index developed by the department of pediatric dentistry at the New Jersey Dental School.
Table 1. Correlation of plaque, gingival indices and disease status with CD4 lymphocyte count (N = 60)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Patients (N = 60)</th>
<th>% Plaque Index</th>
<th>Gingival Index</th>
<th>CD4 Counts/mm²*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy gingiva</td>
<td>5 (8%)</td>
<td>22 ± 34</td>
<td>0.0</td>
<td>1357 ± 693</td>
</tr>
<tr>
<td>Conventional gingivitis</td>
<td>27 (45%)</td>
<td>47 ± 23</td>
<td>1.29 ± 0.5</td>
<td>486 ± 446</td>
</tr>
<tr>
<td>Linear gingival erythema</td>
<td>23 (38%)</td>
<td>55 ± 25</td>
<td>1.64 ± 0.5</td>
<td>333 ± 415</td>
</tr>
<tr>
<td>HIV periodontitis</td>
<td>5 (8%)</td>
<td>94 ± 9</td>
<td>2.80 ± 0.3</td>
<td>35 ± 40</td>
</tr>
</tbody>
</table>

*All values are mean ± 1 SD.

Only the labial surfaces were scored, with each tooth surface divided into five sections: mesial, distal, gingival middle, middle middle, and occlusal middle. Each of the five sections was examined for the plaque presence (score = 1) or absence (score = 0). The individual scores for the four teeth were totaled (range 0-20) and then multiplied by 5 to give a percentage of plaque on all four teeth.

Linear gingival erythema (LGE) was diagnosed as a distinct red linear band of erythema extending 2-3 millimeters apically from the free gingival margin. An additional criterion was the lack of attachment loss and pocketing. The diagnosis was confirmed by the failure to respond to conventional therapy consisting of the removal of plaque and calculus, as well as the use of Peridex® (Proctor & Gamble, Cincinnati, OH) for 1 month.

Periodontal disease was diagnosed based upon the extreme aggressiveness of the lesion. Clinically, this was manifested by attachment loss, spontaneous bleeding, severe inflammation, and radiographic evidence of moderate to severe bone loss. Pain and fever were also universal observations. Only one subject demonstrated moderate to severe ulceration and necrosis of the attached gingiva, however, all five subjects with periodontal disease had at least several areas of soft tissue necrosis. Of the five patients with periodontal disease only one satisfied the criteria for necrotizing ulcerative periodontitis. Consequently, these subjects were not labeled according to the current EC Clearinghouse categories, and the term HIV-associated periodontal disease is used.

Laboratory

For this study, CD4 lymphocyte counts were obtained within 3 months of oral examination with the exception of one subject whose counts were obtained 6 months later. Since the age range of subjects was 1-18 years, the CD4 levels used were with the following reference ranges: 24-60 months, absolute CD4 count 900-2860/mm², and older than 60 months, 689-1566/mm².

Data analysis

The data were analyzed for statistical differences between groups with a one-way analysis of variance F test and the Tukey-Kramer multiple comparisons q-test and with the unpaired t-test. The 95% level (P < 0.05) was selected for statistical significance.

Results

The findings of this study appear in Table 1. Subjects are separated into four groups according to health of the gingiva or periodontis. Table 1 reports the mean plaque index, gingival index, and CD4 counts/mm² for each group. Subjects with healthy gingiva had significantly less plaque (22%) than those with diseased gingiva (47%; P < 0.05, F = 13.1). There were no differences in plaque between subjects with conventional gingivitis (47%) and those with linear gingival erythema (55%; P > 0.05, q = 2.1). However, both groups had significantly less plaque than subjects with HIV-periodontitis (94%). The gingival indices of all four groups differed significantly (P < 0.05, F = 41.0). Healthy subjects had a mean gingival index of 0.0. Those subjects with conventional gingivitis had a mean index of 1.29, those with linear gingival erythema had an index of 1.64, and those with periodontitis were most severe with an index of 2.8 compared to a maximum of 3.0. The CD4 counts/mm² were significantly different among the four groups (P < 0.05, F=14.6), however, they were most different between those with healthy gingiva with high counts (1357) and the other groups with relatively low counts (486, 333, and 35), (P > 0.05, q = 7.3, 8.4 and 8.5). There were no significant differences between those with conventional gingivitis and those with linear gingival erythema (P > 0.05, q = 2.2), or between those with gingival erythema and those with periodontitis (P > 0.05, q = 2.5).

Table 2 differentiates subjects according to the absence or presence of candidiasis. The 19 subjects (32%)
with candidiasis had significantly lower CD4 counts (287) than the 33 subjects without oral disease (705); (P < 0.05, t = 2.80).

Table 3 differentiates subjects according to the absence or presence of any soft tissue oral disease associated with HIV infection, including linear gingival erythema, HIV-periodontitis, herpes simplex, or candidiasis. The 27 subjects with oral disease had significantly lower CD4 counts (287) than the 33 subjects without oral disease (705); (P < 0.05, t = 2.80).

### Discussion

This study demonstrates that medically well-managed, HIV-infected children usually have significant oral disease. Since almost 50% of the subjects exhibited some soft tissue oral manifestations of the HIV infection, oral findings may suggest the presence of disease. Oral candidiasis occurred in one-third of the subjects, which was similar to the prevalence previously reported. In addition, the candidiasis occurred in subjects whose CD4 lymphocyte counts (except for one subject) were less than 1000/mm³. This finding suggests that the relationship of low CD4 counts and occurrence of oral candidiasis should be investigated further.

It has been reported that linear gingival erythema (LGE) is a characteristic oral manifestation of HIV infection in adults, and the prevalence of this condition in intravenous drug users has been estimated to be as high as 49%. In this study of young children, LGE was found to be present in 38% of the subjects, whereas other studies reported a lower prevalence. The difference in prevalence of LGE may be related to the levels of immunosuppression in the subjects of the various studies.

In this study, there was an association between CD4 counts and the severity of periodontal disease, which suggests that periodontal disease may be associated with immunological dysfunction rather than local factors. This suggestion is supported by the finding of a similar plaque index in conventional gingivitis and LGE.

The finding of HIV-periodontitis in 8% of the sample is less than that reported in adults infected with HIV. This may be due to the multiple antibiotics and intravenous gamma globulin prescribed for HIV+ children and these agents may help to prevent periodontal disease. In addition, the epidemiology of periodontitis differs in adults and children. Adults will frequently have a pre-existing conventional periodontal disease at the time of the HIV infection. In both adults and children who are HIV+, the underlying problem is an irregular host response to the oral microflora.

Although it is well established that profound wasting occurs subsequent to HIV infection, neither the prevalence nor the severity of endocrine dysfunction can totally explain the wasting observed in children. Oral lesions may have an important impact on the nutritional status of these children by reducing the food intake. Symptomatic treatment of oral soft tissue lesions may improve food intake thereby reducing generalized wasting. This influence should be studied further.

### Conclusions

1. Medically well-managed children infected with HIV usually have significant oral disease.
2. Gingivitis in HIV-positive children is associated with poor oral hygiene.

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Excess lead exposure associated with increased risk for antisocial and delinquent behavior

Children with high bone lead levels tend to be more aggressive and antisocial, according to an article in a recent issue of The Journal of the American Medical Association.

Herbert L. Needleman, MD, from the Department of Psychiatry, University of Pittsburgh School of Medicine, and colleagues conducted a study to evaluate the association between body lead levels and social adjustment.

The authors write: “In this study, male children considered asymptomatic for lead toxicity with elevated bone lead levels at 11 years of age were judged by both parents and teachers to be more aggressive, have higher delinquent scores, and have more somatic complaints than their low-lead counterparts.

“The subjects themselves reported lead-related increases in antisocial acts at the same age. High-lead subjects were more likely than low-lead subjects to worsen on all scores of parents’ and teachers’ Child Behavior Checklist (CBCL) during the 4-year observation period.”

The study included 301 public school boys whose lead levels were determined by X-ray fluorescence of the tibia. The other outcome measures included the CBCL, teachers’ and parents’ reports, and subjects’ self-report of antisocial behavior and delinquency at 7 and 11 years of age.

At 7 years, borderline associations between teachers’ aggression, delinquency, and externalizing scores and lead levels were observed after adjustment for covariates. At 11 years, parents reported a significant lead-related association with the several CBCL cluster scores.

The researchers write: “The appearance of lead-related effects at the median bone lead level suggests that in some samples lead may contribute to dysfunction in an appreciable proportion of the community.

“These data argue that environmental lead exposure, a preventable occurrence, should be included when considering the many factors contributing to delinquent behavior.”