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Oral findings in HIV-seropositive children

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Abstract

The oral findings in 47 HIV-seropositive children are reported. The patient population consisted of 25 females and 22 males ranging in age from 3 months to 6.5 years. All patients were born to HIV-seropositive mothers. CDC classification of the patients indicated that 26 were P–O, 11 were P–1, and 10 were P–2 (eight of the P–2 patients met CDC criteria for AIDS). Oral candidiasis was the most common finding (six of 26 P–O patients and six of 10 P–2 patients). Only one patient each presented with parotid swelling and gingivitis. Mucosal lesions characteristic of viral infection were not observed in any of the patients.

Introduction

HIV infection has significant oral manifestations in adult patients (Pindborg 1989). Certain oral lesions may be among the earliest clinical signs of HIV infection and disease progression in adults (Klein et al. 1984; Greenspan et al. 1987). However, the incidence, progression, and prognostic implications of oral lesions in HIV-seropositive children are not yet well documented (Falloon et al. 1989; Leggott 1989; Pizzo 1990). This report describes the oral lesions observed in a group of 47 HIV-seropositive pediatric patients.

Methods

Patient Population

The patient population consisted of 47 HIV-seropositive children who were evaluated at the Children's National Medical Center (CNMC) between August, 1989 and October, 1989. All were patients of the Special Immunology Clinic at CNMC. Seropositivity was defined as repeatedly positive ELISA (HIV) confirmed by Western Blot (DuPont). The patient population was comprised of 25 females and 22 males ranging in age from 3 months to 6 1/2 years. All of the patients were born to HIV-seropositive mothers. CDC classification of the patient population indicated that 26 patients were P–O (mean age: 7 months; age range: 4 to 14 months); 11 patients were P–1B (mean age: 3 years, 4 months; age range: 2 years, 1 month to 6 years, 6 months); and 10 were P–2 (mean age: 1 year, 6 months; age range: 3 months to 5 years, 4 months) of which three were P–2D1D3, two were P–2AD1F, two were P–2A, and one each was P–2CD3F, P–2AD1D3, and P–2AD1D3F (Fig 1, next page). At the time of their oral evaluation, none of the patients had received acyclovir or azidothymidine (AZT). Two patients (both P–1B) were being treated with intravenous gamma globulin, and one patient (P–2ADIF) was receiving antiretroviral therapy with dideoxyinosine (ddI).

Oral Evaluations

All patients received an oral evaluation (as a component of their comprehensive medical evaluation) consisting of a clinical examination and indicated dental radiographs. In addition, 14 patients received follow-up examination(s). Each oral evaluation was performed by two of the authors. There were no interexaminer disagreements.

Findings

Oral Candidiasis (OC)

The most common oral lesion in the patient population was oral candidiasis (OC). A diagnosis of OC was based on the presence of creamy white or yellowish plaques overlying a red or normal-colored mucosa, coupled with the presence of positive *Candida* cultures from debris obtained from those lesions. Utilizing these criteria, six of 26 P–O patients and six of 10 P–2 patients had OC. Of the 10 P–2 patients, one had lymphocytic interstitial pneumonitis (C) and 7 had an AIDS-defining infection (D1). Six of these eight patients had OC. OC usually affected large areas of the oral mucosa in the P–2 patients, whereas OC lesions in the P–O patients were generally small and localized. Lesions that are clinically

characteristic of the atrophic (erythematous), hyperplastic, or angular cheilitis types of OC were not observed in any of the patients (Pindborg et al. 1987).

The relationship of absolute CD4 lymphocyte counts and CD4:CD8 lymphocyte ratios to the differences in the severity and frequency of OC observed in the two groups (P–0 and P–2) was analyzed. These data are presented in Table 1. Inspection of these data indicated that as CD4 lymphocyte depletion progressed, the frequency and severity of OC increased. However, the data demonstrated no consistent intragroup correlation between risk for OC and absolute CD4 lymphocyte counts or CD4:CD8 lymphocyte ratios.

Initially, OC was treated with nystatin by having the parent or guardian apply 500,000 units of the drug directly to the oral mucosa with a cotton swab QID. Lesions resolved in five of the six P–O patients after one to four weeks of continuous nystatin therapy (the sixth patient was not available for follow-up evaluation). In contrast, OC lesions in the P–2 patients generally were refractory to topical nystatin therapy. Only variable therapeutic success was achieved in this group (P–2) with ketaconozole (5 to 10 mg/kg/day in one PO dose for one to three weeks).

Representative colonies were isolated from all positive cultures and transferred to a Uni-Yeast-Tek Screen™ (Flow Laboratories; currently available from REMEL, Inc., Lenexa, KS 66215) for speciation. All of the isolates were *Candida albicans*.

Gingivitis

Thirty-one of the 47 patients were dentate. Evaluation of the gingiva of these 31 patients was restricted to visual inspection. A diagnosis of gingivitis was based on the presence of reddening of the gingiva. Utilizing this criteria, only one patient (P–2AD1F) presented with gingivitis. The gingivitis was intensely erythematous and involved the labial marginal and attached gingiva and alveolar mucosa of the four maxillary primary incisors. A swab specimen of this lesion was cultured and demonstrated dense growth of *C. albicans*. Pending culture results, the patient was treated with vigorous oral hygiene. No improvement was noted after 10 days of continuous oral hygiene. Topical nystatin therapy then was initiated, and the lesion demonstrated marked improvement after seven days.

Parotid Swelling

One of the patients (P–2A) had bilateral swelling of the parotid glands. The parotid swellings first were noted several months prior to oral evaluation and were

- P-O[1] Indeterminate infection in perinatally exposed children less than 15 months of age who have antibody to HIV
- P-1 Asymptomatic infection
  - A[2] Normal immune function
  - B Abnormal immune function (hypergammaglobulinemia, T4 lymphopenia, decreased T4/T8 ratio, absolute lymphopenia)
  - C Immune function not tested
- P-2 Symptomatic infection
  - A Nonspecific findings (two or more persisting greater than two months: fever, failure-to-thrive or weight loss of more than 10% of baseline, hepatomegaly, splenomegaly, generalized lymphadenopathy (nodes 0.5 cm in two sites; bilateral counts as one site), parotitis, recurrent or persistent diarrhea (three loose stools/day); two episodes with dehydration within two months)
  - B Progressive neurologic disease (loss of developmental milestones or intellectual ability, impaired brain growth with acquired microcephaly or brain atrophy on CT or MRI, or progressive symmetrical motor deficits with two of the following: paresis, abnormal tone, pathologic reflexes, ataxia, gait disturbance)
  - C Lymphoid interstitial pneumonitis (historically confirmed or bilateral reticulonodular interstitial infiltrates with or without hilar adenopathy for months, unresponsive to antimicrobial therapy, not due to specific infectious pathogens)
  - D Secondary infectious diseases
    - D-1[3] Those listed in CDC definition of AIDS
    - D-2 Recurrent serious bacterial infections (two in a two-year period: sepsis, meningitis, pneumonia, abscess of an internal organ, bone/joint infections)
    - D-3 Others (oral candidiasis persisting two months, recurrent herpes stomatitis, multidermatomal or disseminated herpes zoster)
  - E Secondary cancers
    - E-1 Those listed in CDC definition of AIDS
    - E-2 Others
  - F Other diseases possibly due to HIV infection (hepatitis, cardiopathy, nephropathy, anemia, thrombocytopenia, dermatalogic disease).

[1] Class, [2] Subclass, [3] Category

Fig 1. CDC classification system for HIV infection in children less than 12 years of age.

characterized by slow, continuous enlargement. They caused marked facial disfigurement, were firm but painless, and were not associated with xerostomia.

Other Findings

One patient (P–1B) presented with a unilateral swelling of the floor of the mouth with the clinical characteristics of a ranula — namely, it resembled the bloated, translucent underbelly of a frog. The lesion was painless and did not interfere with feeding or speech. In addition, two patients presented with dental anomalies. Teeth r and q were fused in one patient (P–1B) and teeth n and o were fused in another patient (P–O).

Discussion

Oral candidiasis (OC) is a common finding in adults with AIDS (Silverman et al. 1986: Syrjanen et al. 1988). In this regard, eight of the 10 P–2 patients of this report had either an AIDS-defining infection (seven patients) or lymphocytic interstitial pneumonitis (one patient) and therefore were classified as having AIDS. Six of these eight patients presented with OC, indicating that this lesion is a common finding in young children with AIDS.

OC often is resistant to topical antifungal agents in adult AIDS patients (Babajews et al. 1985). Likewise, the clinical findings of this report indicate that OC frequently is resistant to topical antifungal therapy in young pediatric AIDS patients. In this regard, two of the AIDS patients with OC developed pharyngeal and esophageal extensions while being treated actively with nystatin. One of these two patients required hospital admission and IV amphotericin B therapy. The other patient was managed with ketaconozole which was discontinued prematurely due to hepatotoxicity. Clearly, nontoxic antifungal agents are needed to prevent and treat OC in HIV-infected pediatric patients.

OC also has been described as having prognostic significance in HIV-seropositive adults as a predictor for heralding the progression of the disease to full-blown AIDS (Chandrasekar and Molinari 1985). The potential predictive value of OC in young HIV-seropositive pediatric patients currently is not known. In this regard, the presentation of OC in P–O patients may have predictive value in differentiating positive HIV serology due to infection vs. maternal antibody. Although OC may present in healthy infants (independent of HIV infection) during the neonatal period, its presence in a healthy infant more than 3 months of age is rare. Accordingly, it is interesting to note that all six of the P–O patients with OC in this report were 4 months of age or older.

Four types of OC have been recognized in HIV-infected adults:

1. Pseudomembranous
2. Hyperplastic
3. Atrophic (erythematous)
4. Angular cheilitis (Pindborg et al. 1987).

The OC lesions observed in this report were all clinically characteristic of the pseudomembranous type. One possible explanation for this observation is that atrophic OC may be overlooked easily.

HIV gingivitis has been reported in adult patients as a characteristic oral manifestation of HIV infection (Winkler et al. 1988). The presence of *Candida* is a frequent finding when plaque samples from HIV gingivitis in adults are cultivated (Winkler et al. 1988). Clinical observations indicate that successful treatment of HIV gingivitis in adults frequently is dependent on including antifungal therapy as an additional therapeutic component to conventional plaque-control measures (Winkler et al. 1988). In this regard, the one patient (P–2ADIF) that presented with gingivitis in this report had *Candida* isolated from the lesion and did not respond to conventional treatment until anti-fungal therapy was initiated. In addition, it is of interest to note that this child was being treated with ddI and was the most severely immunocompromised patient in the study population (absolute CD4 lymphocyte count = 35; CD4:CD8 lymphocyte ratio = 0.1).

Parotid swelling has been reported to occur in 5% of seropositive homosexual men (Silverman et al. 1986). A recent commentary indicated that 20% of HIV-infected children have unilateral or bilateral involvement of the parotid glands (Leggott 1989). Only one patient in this report presented with this complication.

None of the patients presented with oral mucosal lesions characteristic of viral infection. In particular, lesions characteristic of herpes simplex virus infection or Epstein-Barr virus infection (e.g.: hairy leukoplakia) were not identified in any of the patients. These observations coupled with other reports (Andriolo et al. 1986; Silverman et al. 1986) suggest that these types of lesions occur less frequently in young HIV-infected children

Table 1. Relationship of OC to CD4 Counts and CD4:CD8 Ratios

CDC Grop	*Number of Patients*	*(%) Proportion of Patients with OC*	*CD4 Count*		*CD4:CD8 Ratio*	
			Mean	*Range*	*Mean*	*Range*
P–0	26	(23%) 6+	3220	1594–4836	1.96	0.9–3.7
		20–	3501	2116–4103	2.28	1.3–3.3
P–2	10	(60%) 6+	1357	35–4873	1.18	0.1–2.68
		4–	1244	482–2381	0.81	0.4–1.5

as compared to HIV-infected adults. It is possible that these observations in part reflect differences in exposure to viral agents.

In summary, this limited cross-sectional report indicates that OC is a common and serious complication of HIV infection in young children. In addition, the relative infrequent presentation of gingivitis coupled with the absence of viral oral mucosal lesions suggests that the oral presentation of HIV infection in young children is different than adults.

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Short-term life expectancies for many AIDS victims improving

Victims of the most common AIDS-related infection have much better short-term life expectancies now than just a few years ago, according to reports in the January 19, 1990 issue of the *Journal of the American Medical Association.*

Two studies in this issue reach the same conclusion: adults diagnosed with pneumocystis carinii pneumonia (PCP—the most common AIDS-related infection) have significantly better short-term survival rates today than adults diagnosed in the early 1980s. One study reviewed cases in San Francisco; the other was national in scope.

"The data in these reports appear to confirm what clinicians, investigators, and patients have known for several years: life after AIDS is improving and death is no longer as swift and as certain as in the early years of the epidemic," wrote Richard E. Chaisson, MD, of the Johns Hopkins School of Medicine, Baltimore, MD, in an accompanying editorial.

In the national study, those adults whose PCP was among the first signs of AIDS, there was a dramatic improvement in short-term survival rates between 1984 through 1987, wrote Jeffrey E. Harris, MD, PhD, of the Department of Economics, Massachusetts Institute of Technology, Cambridge.

In 1984, the one-year survival rate was 39.1%. That number jumped to 48.4% for those diagnosed with PCP in 1986 and 1987.

The San Francisco study, written by George F. Lemp, DrPH, of the AIDS Office, Department of Public Health, City and County of San Francisco, CA, and his colleagues, found similar heartening trends.

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