

Infective Dermatitis Associated with the Human T Cell Lymphotropic Virus Type I in Salvador, Bahia, Brazil

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Background. Infective dermatitis associated with human T cell lymphotropic virus type I (HTLV-I) infection is a chronic, relapsing eczema of childhood.

Methods. Children, their mothers, and their siblings underwent serological testing for HTLV-I. Epidemiological data were collected from all seropositive children and their family members, and clinical and dermatological examinations were performed. Laboratory studies, including skin culture, and histopathological analyses were also performed. The diagnosis of infective dermatitis associated with HTLV-I (IDH) was made according to previously established criteria.

Results. All of the patients with cases that demonstrated clinical aspects of IDH were positive for HTLV-I. The median age of the children at the time of the first visit was 8.0 years (range, 2–14 years). The median duration of breastfeeding for 19 children was 22.5 months (range, 1–48 months). The lesions were erythematous, scaly, exudative, and crusted in all cases. The scalp, retroauricular areas, neck, and groin were the regions that were commonly affected. Cultures were positive for *Staphylococcus aureus* for 95% of the patients. The children were followed-up for a median of 3.0 years (range, 0.1–7 years), and 5 children developed HTLV-I-associated myelopathy/tropical spastic paraparesis. All of the children except 1 were treated with sulfamethoxazole-trimethoprim, and their lesions either improved greatly or completely disappeared.

Conclusions. The present study demonstrates the severity of IDH in Bahia and confirms that its diagnosis is based almost exclusively on clinical aspects of the disease. Serological testing for HTLV-I and careful follow-up is recommended for all children with chronic, relapsing, severe eczema in regions where HTLV-I is endemic.

In 1966, Sweet [1] observed a severe form of infected childhood eczema in Jamaica that he called infective dermatitis. The lesions were infected from the time of onset and were located on the face, scalp, and neck. One year later, Walshe [2], also in Jamaica, described a series of 25 children with this type of eczema who underwent clinical and bacteriological study. In 1990, infective dermatitis was first reported to be related to the human T cell lymphotropic virus (HTLV-I) [3]. In

1998, La Grenade et al. [4] proposed the new designation of infective dermatitis associated with HTLV-I (IDH) and the major and minor criteria for diagnosis.

Cases of IDH have been reported in Trinidad and Tobago, Colombia, the Dominican Republic, Peru, French Guyana, and Africa [5–10]. In Brazil, an isolated case of IDH was reported in 1996 [11]. In Japan, where the frequency of HTLV-I carriers is high, only 3 cases of IDH have been reported [12]. Some authors have linked IDH to the development of adult T cell leukemia/lymphoma and HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP) [12, 13].

HTLV-I is endemic in Salvador (Bahia, Brazil), an area with the highest prevalence of this infection among blood donors in Brazil [14]. Recently, the overall prevalence of HTLV-I infection in the general population in Salvador was estimated to be 1.76% [15].

The objectives of the present study were to establish

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the frequency of IDH in a dermatology outpatient clinic and to study the epidemiological and clinical aspects of 23 cases. Up to the time of this study, only 1 case of IDH had been reported in the state of Bahia, Brazil [16].

MATERIALS AND METHODS

The study population consisted of children of low socioeconomic status, aged 1.5–15 years, who attended the dermatology outpatient clinic of the Federal University of Bahia. Between August 1997 and September 1999, all of the children with chronic eczema who visited the clinic without a referral, as well as the mothers of these children, underwent serological testing for HTLV-I in a preliminary study of the prevalence of IDH. Between September 1999 and December 2002, the serological screening was performed only for children who had already received a clinical diagnosis of IDH.

In all cases, antibodies to HTLV-I and HTLV-II were detected by diagnostic ELISA (Cambridge Biotech) and were confirmed by Western blotting, which is capable of discriminating between HTLV-I and II (HTLV Blot 2.4; Genelab Singapore). Serological testing for HIV was also performed for HTLV-I-positive patients.

Epidemiological data were collected for all HTLV-I-positive children. Clinical and dermatological examination of the children and of their HTLV-I-positive siblings was performed. Patients with simultaneous involvement of the scalp, neck, trunk, and limbs were considered to have disseminated lesions.

Patients underwent routine laboratory studies and measurement of serum levels of IgA, IgE, IgG, and IgM. In addition, swabs from skin were cultured for bacterial pathogens by use of routine methods, and a direct mycological examination was also performed. In all cases, a punch skin biopsy of the scalp lesion was performed. Biopsies were performed to exclude the presence of other diseases.

The diagnosis of IDH was made according to previously established criteria [4]. A differential diagnosis between IDH and atopic dermatitis was made on the basis of preexisting criteria [17–19], and a differential diagnosis between IDH and seborrheic dermatitis was made on the basis of clinical findings [20, 21]. Follow-up was based on the reappearance of clinical symptoms, which were identified during clinical and dermatological reevaluation that occurred when routine laboratory examinations were performed.

The protocol of the present study was approved by the Research Ethics Committee of the Professor Edgard Santos Teaching Hospital. The parents or legal guardians of the children gave their signed, informed consent for their child's participation.

RESULTS

Between September 1997 and August 1999, a total of 43 patients aged 1.5–15 years with chronic eczema were seen. Diagnoses included 27 cases of atopic dermatitis (62.9%), 9 cases of IDH (20.9%), and 7 cases of seborrheic dermatitis (16.2%). After August 1999, an additional 14 patients with IDH were seen. No HTLV-I-seropositive patients with atopic or seborrheic dermatitis were observed. No differences were observed in the clinical features of disease, median ages, and sex distribution between patients who received diagnoses of IDH during each of these 2 periods. The study sample consisted of 23 patients with IDH: 15 female patients (65.2%) and 8 male patients (34.8%), of whom 14 were multiracial (60.9%) and 9 were black (39.1%). Seventeen patients (73.9%) were from Salvador, and 6 (26.1%) were from neighboring towns. The median age of the children at first visit was 8.0 years (range, 2–14 years). The median age at onset of the disease was 1.4 years (range, 0.2–6 years). All of the children came from low socioeconomic backgrounds. In 10 patients (43.5%), the skin lesions appeared before 18 months of age. In the case of a child who had been abandoned, the age of the child at the onset of the disease was not known, and the epidemiological data were missing. Twenty-two children had no history of sexual activity or sexual abuse before the onset of the disease, and information about sexual history was missing for 1 child.

Previous history of atopy was noted in 2 cases (8.6%), and family history of atopy was noted in 10 cases (43.5%). All patients complained of pruritus of moderate intensity. The following conditions were observed at baseline or during follow-up: otitis in 11 patients (47.8%), scabies in 10 (43.5%), acquired ichthyosis in 3 (13.0%), vulvovaginitis in 2 (8.7%), molluscum contagiosum in 2 (8.7%), and corneal ulcer in 1 (4.3%).

Only 20 of the mothers underwent serological examination for HTLV-I; 1 mother had 2 children enrolled in the study, 1 child was abandoned at birth, and the mother of another child in the study was dead. A total of 17 of the 20 mothers tested positive. All of the women were asymptomatic carriers, except for 1 mother who presented with HAM/TSP. One mother who was an asymptomatic carrier had a history of severe childhood eczema that had occurred up to the age of 15 years. Forty-one siblings of children with IDH underwent serological testing, and 6 were HTLV-I carriers.

Twenty-two children (95.6%) were breastfed, but the duration of breastfeeding was unknown for 3 children. The median duration of breastfeeding in the other 19 cases was 22.5 months (range, 1–48 months). Of the 3 children of seronegative mothers, 2 were breastfed by other women, and 1 had a history of blood transfusion.

Dermatological examination. The most frequent sites of skin involvement were as follows: scalp (in 100% of patients; figure 1), retroauricular areas (in 100% of patients), neck (in



Figure 1. Severe involvement of scalp, forehead, and external ear, with exudative and crusted lesions

91.3% of patients; figure 2) and groin (in 91.3% of patients; figure 3). The antecubital fossae were affected in 73.9% of patients (figure 3 and table 1). In 14 children (60.8%), the skin lesions were disseminated. Skin lesions were erythematous, scaly, and exudative with adherent yellowish crusts. Lichenified lesions and papules were also seen. Retroauricular fissures, disseminated follicular papules, and pustules were observed in most patients (table 2). Crusting of the nostrils was observed in 19 patients (figure 4), and nasal discharge was observed in 5 patients. Blepharoconjunctivitis was observed in 14 patients (60.9%). Acquired ichthyosis was present in 3 patients.

Laboratory studies. A complete blood cell count was performed for 20 patients. Hemoglobin levels ranged from 10.5 to 13.9 g/dL. Mild anemia (defined as a hemoglobin level of <12 g/dL) was detected in 60% of the cases. WBC and differential cell counts were within the normal ranges. Immunoglobulin levels were measured for 18 patients. IgA and IgM levels were within the normal ranges. High levels of IgE were observed in 55.5% of the patients. IgG levels were within the normal ranges in 16 patients, and, in 2 patients, low levels were observed. All of the patients were seropositive for HTLV-I and were seronegative for HIV. Skin cultures were performed for 19 patients and were positive for *Staphylococcus aureus* in 18 patients (94.7%); in 2 patients (11.1%), a simultaneous infection with β -hemolytic *Streptococcus* was observed. Direct mycological examination performed for 19 patients was negative for dermatophytes and *Pityrosporum* species in all cases.

Stool microscopy was performed for 17 patients, 14 (82.4%) of whom had positive results for at least 1 parasite. In 5 patients

(35.7%), both *Ascaris lumbricoides* and *Trichuris trichiura* were observed. *Enterobius vermicularis* was observed in 3 cases (21.4%), *Giardia lamblia* and *Strongyloides stercoralis* were observed in 2 cases each (14.3%), and *Entamoeba histolytica* and *Ancylostoma* species were observed in 1 case each (7.1%).

Evolution and treatment. The patients were followed-up for a median of 3.0 years (range, 0.1–7.0 years). With the exception of one child who was allergic to sulfonamides, all patients were treated with systemic sulfamethoxazole-trimethoprim (40 mg/kg q24h of sulfamethoxazole and 8 mg/kg q24h of trimethoprim) for 15 days, and, thereafter, received a one-half dose at night until the disease was controlled. Antihistamine drugs, topical corticosteroids, and emollients were also prescribed. Erythromycin was used to treat the child who was allergic to sulfonamides, and an excellent response was achieved.

Of the 14 patients who presented with disseminated lesions, partial control was achieved for 7, but these patients continued to experience frequent relapses with disseminated exudative lesions whenever treatment was stopped. Four of them eventually developed HAM/TSP (J.R.L. Primo, personal communication). Of the 7 other patients, 1 presented with no additional lesions by the age of 13 years, and 6 exhibited sporadically relapsing scaly lesions without exudation either on the scalp and/or in the retroauricular areas. Two patients who had not presented with crusts in the nostrils at baseline presented with this feature during relapses.

Of the 9 patients with localized lesions, 3 presented with complete disappearance of the lesions by the age of 12–13 years, and 4 continued to present with sporadically relapsing ery-



Figure 2. Erythematous, scaly, exudative, and crusted lesions in retroauricular areas and on neck and scalp. Note erosions on scalp.

thematous, scaly lesions without exudation either on the scalp or in the retroauricular areas. One of these patients developed HAM/TSP. Two were lost to follow-up.

DISCUSSION

Twenty-three patients with IDH were identified, and all of them were seropositive for HTLV-I. In 10 patients, the symptoms probably appeared earlier than is usually reported in the literature (i.e., the patients were aged <1 year) [1, 2, 4]. However, there are some reports of IDH in patients as young as 6 months of age [7]. The predominance of female patients in these cases is in agreement with the literature [22]. In the present study, the transmission of the HTLV-I infection certainly occurred vertically, probably as a result of prolonged breastfeeding, except in one case in which the child, whose mother was seronegative, had received a blood transfusion. This observation demonstrates that IDH may result from an infection that is acquired through blood transfusion.

The most frequent pathway of vertical transmission of HTLV-I is breastfeeding. Serological surveys of the breastfed children of women who are carriers have reported infection rates varying from 15.4% to 25%, and the surveys indicate that the rate of transmission is directly proportional to the duration of breastfeeding. However, bottle-fed children may also become vertically infected. Considering that, in the majority of the cases we report, the duration of breastfeeding was >8 months, the route of transmission of the infection was probably lactogenic.

In one child who was breastfed for 2 months, vertical transmission could have occurred by breastfeeding or by other means (e.g., transplacentally or in the birth canal) [23].

Seropositivity for HTLV-I is not the only criterion for the diagnosis of IDH. There have been reports of other kinds of eczema linked to HTLV-I, such as atopic and seborrheic dermatitis [4, 24, 25]. La Grenade et al. [4] diagnosed atopic dermatitis in 14% of children with HTLV-I. Seborrheic dermatitis associated with HTLV-I has been observed in children and adults [25, 26]. Thus, it is important to make a careful differential diagnosis [17–21]. The sites characteristically involved in atopic dermatitis of childhood are the antecubital and popliteal fossae, the sides of the neck, the wrists, the ankles, and the dorsa of the hands and feet. In adults, the picture is similar, with lichenification of the flexures and hands, in particular [19, 20]. In IDH, the morphology and distribution of the lesions are similar, in part, to those of atopic dermatitis, although, in IDH, the lesions are more marked, are exudative, and are more exuberantly infected and fetid. Besides, in IDH, crusts are detected in the nostrils, and fissures are found behind the ears, and IDH is sometimes associated with blepharoconjunctivitis. In addition, fissures in atopic dermatitis are seen mainly in cases occurring in infancy [18]. The pruritus observed in atopic dermatitis is more marked than that found in IDH.



Figure 3. Eczematous dermatitis with diffuse erythema and scaling in the antecubital fossae and groin.

Table 1. Distribution of lesions due to infective dermatitis associated with HTLV-I.

Localization	No. (%) of patients (n = 23)
Scalp	23 (100)
Retroauricular areas	23 (100)
Neck	21 (91.3)
Groin	21 (91.3)
Paranasal area	20 (86.9)
Axillae	20 (86.9)
External ear	19 (82.6)
Nostrils	19 (82.6)
Forehead	17 (73.9)
Umbilicus	17 (73.9)
Antecubital fossa	17 (73.9)
Perioral area	15 (65.2)
Trunk	14 (60.9)
Abdomen	14 (60.9)
Popliteal fossa	13 (56.2)
Limbs	12 (52.2)
Genital area	12 (52.2)
Buttock	9 (39.1)

Seborrheic dermatitis is rare before puberty [21]. The condition known as seborrheic dermatitis of infancy is generally confined to the first months of life. In seborrheic dermatitis of puberty, the lesions are erythematous and scaly and occur primarily on the scalp and face and in the postauricular, presternal, and intertriginous areas [20, 21]. Although sometimes occurring in those same regions, the lesions in IDH, in contrast to the lesions found in cases of seborrheic dermatitis, are more exudative and fetid with yellowish crusts. Other points of difference are the presence in IDH of rhinitis, crusting in the nostrils, papular rash, and pruritus. In addition, *Pityrosporum* yeasts, known to occur frequently in seborrheic dermatitis [27, 28], were not observed during direct examination of the lesions occurring in IDH.

The cases studied fulfilled the major criteria of La Grenade et al. [4], except for 3 cases in patients who did not present with chronic nasal discharge and/or crusting in the nostrils. Suite et al. [5] described 15 patients with IDH who had no chronic nasal discharge. Crusting in the nostrils is probably transient, because, in some of the patients we describe, it was only observed during the first visit or during relapses. On the basis of our results, the presence of crusts or rhinorrhea cannot be considered to be an obligatory factor for the diagnosis of IDH; however, it is an important major criterion.

The involvement of the antecubital and popliteal fossae that was frequently seen in the patients we describe is not generally noted in the literature. However, Suite et al. [5] observed this involvement in 33.3% of cases. Although eczema of the ante-

cubital flexures is generally observed in atopic dermatitis, in the patients we describe, the characteristic and extensive involvement of the scalp and retroauricular areas with exudative, crusted, infected, and fetid lesions is strongly indicative of IDH. The pruritus about which all patients complained was not as intense as that expected in atopic dermatitis. The clinical aspects of IDH were so thoroughly characteristic that, after observation of the first cases, the diagnostic hypothesis of this disease was made by the staff before they received the results of serological testing.

Routine laboratory tests are not helpful in the differential diagnosis. One study reported more-marked anemia, lymphocytosis, and an elevated erythrocyte sedimentation rate in IDH [4]. Immunoglobulin levels (IgG, IgA, and IgD) are higher in IDH than in atopic dermatitis, but IgE levels are elevated in both conditions [4]. However, in the cases we report, only mild anemia was found, and lymphocytosis was not observed. In 55% of the cases, IgE levels were high. The findings of histopathologic examination were indistinguishable from those found in cases of other forms of eczema [29].

The association of IDH with other acquired infections is also common among HTLV-I carriers [30–32], although the infections are not necessarily part of the manifestations of IDH. Prolonged use of oral antibiotics is recommended in the literature until puberty, at which time the severity of the bacterial infection seems to lessen [33]. In the patients we describe, a good response to systemic treatment with sulfamethoxazole-trimethoprim was observed. This is another point of distinction between IDH and atopic and seborrheic dermatitis; the latter do not respond to systemic treatment with sulfamethoxazole-trimethoprim. Mahé et al. [7] obtained a good response with this treatment in one case. Relapses always occurred following the withdrawal of the drug treatment, as is noted in the literature with respect to the use of antibiotics. Relapses were more frequent and more severe among the patients with disseminated lesions than among the patients with more-localized lesions. The disease seemed to run a more severe course in the

Table 2. Morphology of skin lesions due to infective dermatitis associated with HTLV-I.

Characteristic	No. (%) of patients (n = 23)
Erythematous, scaly, and exudative lesions	23 (100)
Exudative and crusting lesions	23 (100)
Scaling papules	23 (100)
Lichenified lesions	23 (100)
Retroauricular fissures	19 (82.6)
Crusting of nostrils	19 (82.6)
Disseminated follicular papules	17 (73.9)
Pustules	12 (52.7)



Figure 4. Extensive and severe involvement of scalp, forehead, eyebrows, nasal folds, nostrils, perioral area, and external ear, with exudative lesions and yellow crusts.

first group, because 4 of these patients eventually developed HAM/TSP, but only 1 patient with localized IDH developed this kind of myelopathy.

Without question, IDH possesses some of the characteristic features of both atopic and seborrheic dermatitis; however, it presents some distinctive features, such as the intensity of skin lesions and the presence of infected and crusted skin lesions (including those found in the nostrils), that permit a differential clinical diagnosis. Moreover, the good response of IDH to systemic treatment with sulfamethoxazole-trimethoprim constitutes another differentiating factor.

The frequency of IDH observed in the present study may have been higher than that observed in Jamaica because the data in the present study were collected at a center to which the more severe cases are referred. Previous indirect evidence of the importance of IDH in Bahia was the finding that HTLV-I-positive pregnant women more frequently reported a history of eczema-like IDH in childhood than did a control group of HTLV-I-negative pregnant women [34]. Besides vertical transmission, blood transfusion may constitute another route of infection among IDH patients.

The present study demonstrates the severity of IDH in Bahia. Differentiating the diagnosis of IDH from those of atopic dermatitis and seborrheic dermatitis is important, because therapeutic management of each of these conditions is different. We consider the extended, long-term use of sulfamethoxazole-trimethoprim to be the treatment of choice in cases of IDH.

The present study will certainly contribute toward alerting pediatricians and dermatologists to this important pathology.

The present study is a pioneering evaluation of this subject in Brazil.

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