MAJOR ARTICLE

Infective Dermatitis Associated With Human T-Cell Lymphotropic Virus Type 1: Evaluation of 42 Cases Observed in Bahia, Brazil

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Background. Infective dermatitis associated with human T-cell lymphotropic virus type 1 (HTLV-1; IDH) is a chronic recurrent eczema affecting HTLV-1–infected children. The epidemiological and dermatological characteristics of IDH are described, and their principal diagnostic criteria are reevaluated.

Methods. Forty-two patients were included: 40 patients serologically positive for HTLV-1 and 2 seronegative patients who tested positive in polymerase chain reaction (PCR) assays.

Results. The mean age at onset of the disease was 2.6 ± 2.4 years (range, 2 months–11 years). The mean duration of breast-feeding was 24.2 months. The lesions were erythematous, scaly, and crusted, always affecting the scalp and retroauricular regions. Crusting of the nostrils was observed in 64.3% of the patients. Of the 36 patients followed up, 23 had the active disease. The age at which IDH disappeared in the others was 10–20 years.

Conclusions. The onset of IDH may occur earlier than reported in the literature. The scalp and retroauricular regions are always affected, and lesions are invariably present in ≥3 areas. Crusting of the nostrils cannot be considered an obligatory factor for the diagnosis of IDH. The recurring nature of IDH was a characteristic found in all cases. Patients with classic IDH lesions who are serologically negative should be investigated by PCR. Therefore, the indispensable criteria for diagnosis are (1) presence of erythematous-scaly, exudative, and crusted lesions involving ≥3 areas, including the scalp and retroauricular regions; (2) recurring nature of the lesions; and (3) a finding of HTLV-1 infection by serology or molecular biology.

Human T-cell lymphotropic virus type 1 (HTLV-1) is endemic in various countries, including Brazil. The geographic distribution of HTLV-1 in this country is heterogeneous. On the basis of serological screening in volunteer blood donors in several state capital cities of Brazil, the frequency of HTLV-1 infection ranged from 0.4 cases/1000 population in Florianópolis in the state of Santa Catarina to 10.0 cases/1000 population in São Luís in the state of Maranhão and 9.4 cases/1000 population in Salvador in the state of Bahia [1]. In Salvador, the seroprevalence rate of HTLV-I in healthy persons in the general population is 1.76% [2]. The population in the cities of São Luís and Salvador is largely of African descent.

HTLV-1 was first discovered in 1980 [3]; however, infective dermatitis was described 14 years earlier in Jamaica as a different form of chronic eczema [4]. The 17 cases of infective dermatitis described by Sweet [4] involved severe and frankly infected lesions affecting the ears, face, scalp, neck, and shoulders. According to this author, onset of the disease usually occurs at about the age of 2 years, seldom before 18 months of age. Disseminated, fine follicular papules have also been reported [4]. One year later, Walshe [5] evaluated the bacteriological characteristics of infective dermatitis. In 1990 [6], infective dermatitis was linked to

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HTLV-1 infection, and in 1996, the disease began to be referred to as infective dermatitis associated with HTLV-1 (IDH) [7]. Criteria for the diagnosis of IDH were established in 1998 [8].

IDH is a form of infective, recurrent dermatitis that affects children vertically infected with HTLV-I. The lesions are erythematous, scaly, and crusted and are usually located on the scalp and retroauricular region, neck, groin, paranasal region, axillae, external ear, and nostrils. The patients present with mild to moderate pruritus, with chronic nasal secretion or crusting on the nostrils. The condition is generally associated with *Staphylococcus aureus* and/or *Streptococcus beta haemolyticus* infection [8, 9]. Although crusting of the nostrils is a common finding, it may be absent [9].

IDH may progress to HTLV-1–associated myelopathy/tropical spastic paraparesis (HAM/TSP) [8, 10] and adult T cell leukemia/lymphoma [11, 12]. More recently, cases of late-onset IDH have been described [13, 14]. Only 2 studies have been conducted on the epidemiological and dermatological characteristics of a series of cases of IDH with a confirmed diagnosis and serological positivity for HTLV-1: one in Jamaica, in which 50 patients were evaluated, and the other in Bahia, Brazil, involving 23 cases [8, 9]. Currently, 42 cases have been diagnosed in Salvador, Bahia, Brazil, and the objective of the present study was to reevaluate the dermatological and epidemiological characteristics of IDH and review the principal diagnostic criteria for this disease.

METHODS

Forty-two patients (children and adolescents) who received a diagnosis of IDH at the dermatology outpatient clinic of the Federal University of Bahia since August 1997 were included in this case series study. Twenty-three of these cases have been described elsewhere [9]. Thirty-six patients have been followed up, and the duration of follow-up was 1–12 years (mean, 6.75 ± 3.96 years). HTLV-I infection was detected in the patients and in their mothers by diagnostic enzyme-linked immunosorbent assay (Cambridge Biotech) and confirmed by Western Blot (HTLV Blot 2.4; Genelab Singapore) and/or polymerase chain reaction (PCR) for HTLV-1 in peripheral blood mononuclear cells (PBMCs). Serological testing for human immunodeficiency virus was also performed in the patients. Patients who were serologically negative for HTLV-1 but who had clinical signs of IDH were tested with PCR for HTLV-1 in PBMCs. Epidemiological data were collected, and the patients underwent clinical, dermatological, and neurological examination. Diagnoses of IDH and HAM/TSP were made according to previously established criteria [8, 9, 15]. Patients with simultaneous involvement of the scalp, neck, trunk, and limbs were considered to have the disseminated form of the disease. Routine laboratory studies and skin cultures for bacterial pathogens were performed. In all cases, skin biopsies of the scalp lesion were performed for anatomopathological and immunohistochemical studies. Patients who had had no treatment for a period of >6 months and who presented no signs of the skin disease were considered to be in remission.

RESULTS

The study sample consisted of 27 female patients (64.3%) and 15 male patients (35.7%). All patients were of African descent and came from underprivileged socioeconomic backgrounds. Thirty-two patients (76.19%) were from Salvador, the capital of the state of Bahia, and 10 (23.80%) were from other towns in the same state. There were 2 pairs of siblings. Three patients had been abandoned by their parents and were living in orphanages or on the streets. In 2 of the children who had been abandoned and in another 2 patients, the age of the child at onset of the disease and the duration of breast-feeding were unknown. One patient whose mother was seronegative had a history of a blood transfusion.

The mean age of the patients at first visit to the clinic was 8.9 ± 4.0 years (range, 2–18 years). This information was available for all the patients except 1 orphan. The mean age at onset of the disease was 2.6 ± 2.4 years (range, 2 months to 11 years; this information was available for 38 patients). In 14 (36.8%) of 38 patients, the skin lesions appeared at ≤12 months of life. Duration of breast-feeding was 1–72 months (mean, 24.2 months; based on information from 38 patients). A history of chronic nasal secretion was reported in only 7 patients (16.6%). All patients complained of pruritus of mild to moderate intensity.

In 5 cases, serology was not performed in the patients' mothers because they refused to attend the clinic or to undergo testing. Of the 32 mothers tested serologically, 28 were seropositive and 4 were seronegative. In 2 of these seronegative mothers, the PCR result for HTLV-1 in PBMCs was also negative. In 3 seronegative mothers, the children had been breast-fed by other women. With respect to the other seronegative mother, no information was available on breast-feeding.

Dermatological Examinations

Table 1 shows the topography of the lesions in the 42 patients evaluated at their initial visit to the clinic, in order of frequency. As shown, all patients presented lesions on the scalp (Figure 1) and retroauricular region (Figure 2), whereas crusting of the nostrils (Figure 3) was found in only 27 patients (64.3%); however, in 2 patients, this feature was seen only during relapses. The antecubital and popliteal fossae were affected in 24 patients (57.1%) (Figure 4). Thirty-five patients

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Table 1. Distribution of the Lesions in 42 Patients with Infective Dermatitis Associated With Human T-Cell Lymphotropic Virus

Distribution of Lesions	Patients, No. (%)
Scalp	42 (100)
Retroauricular regions	42 (100)
Neck	37 (88.0)
Axillae	35 (83.3)
Groin	33 (78.6)
Paranasal skin	30 (71.4)
Ears	30 (71.4)
Thorax	27 (64.3)
Abdomen	26 (62.0)
Antecubital and popliteal fossae	24 (57.1)
Eyelids	24 (57.1)
Forehead	23 (54.8)
Perioral region	21 (50.0)
Umbilicus	17 (40.8)
Limbs	15 (35.7)
External genitalia	14 (33.3)
Buttocks	7 (16.6)

(83.3%) had the disseminated form of the disease at the time of diagnosis, without taking into account the fine follicular papules that, when present, were always disseminated. The lesions were severe, fetid, erythematous-scaly, and exudative, covered with adherent yellowish crusts (Figure 1). Other lesions observed consisted of erythematous-scaly papules (Figure 5), follicular papules, and retroauricular fissures (Table 2). Blepharoconjunctivitis was found in 24 patients (Figure 6).

A bacteriological evaluation of the skin lesions was performed in 30 patients. *Staphylococcus aureus* was isolated in 29 patients (96.6%), and an association with *Streptococcus pyogenes* was found in only 2 patients. The findings at

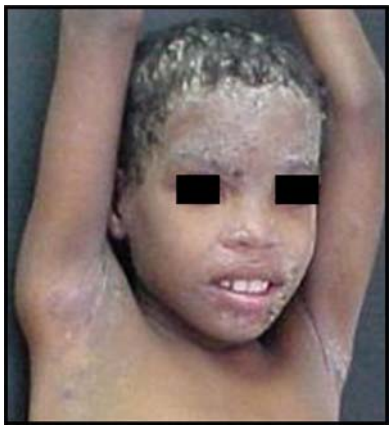

Figure 1. An 8-year-old female with erythematous-scaly-crusty lesions.

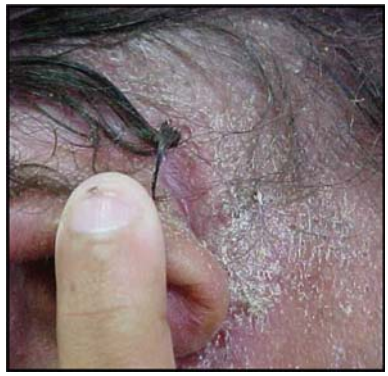

Figure 2. A 9-year-old female with erythematous-scaly lesions on scalp and retroauricular region since 1 month of age.

histology and immunohistochemistry were similar to those already reported [16]. Of the 42 patients who received a diagnosis, 36 continued to be followed up, and the rest have been lost to follow-up. In all of these patients, the relapsing nature of the disease was seen after discontinuation of treatment. Of these patients, 23 (63.8%) have the active disease; however, the disease remains disseminated in only 1. Five of these patients are now >18 years of age; the oldest is 23 years of age. Thirteen cases (36.1%) are in remission. The mean age at which IDH disappeared was 15 years (range, 10–20 years).

The following skin diseases were observed at baseline or during follow-up: scabies in 23 patients (63.8%), 2 of whom had Norwegian scabies; xerosis cutis in 23 (63.8%); and acquired ichthyosis in 4 (9.5%). Of the infectious skin diseases found in these patients, verruca vulgaris, herpes zoster, molluscum contagiosum, genital warts, and onychomycosis were present in <4%.

Seventeen patients (47.2%) with IDH received a diagnosis of HAM/TSP in childhood or adolescence, 9 of these cases

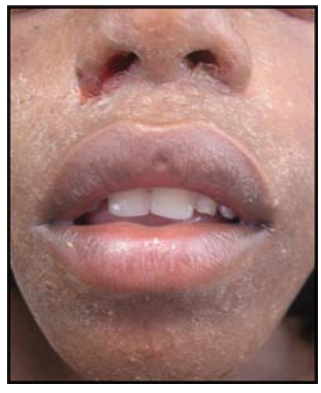

Figure 3. A 12-year-old male with IDH since 11 months of age. Crusting on nostrils with erosion at right.

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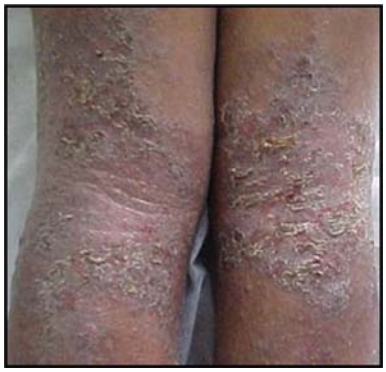

Figure 4. A 6-year-old female with disease since 1 year of age. Erythematous-scaly-crusty lesions on popliteal fossae.

have been reported elsewhere [10]. One of these cases progressed to adult T-cell leukemia/lymphoma; this case has also already been published [12]. Of the 17 patients with HAM/TSP, 14 were given a definitive diagnosis of HAM/TSP, with a probable diagnosis of HAM/TSP in the other 3. Three patients died, 2 of whom had associated HAM/TSP. Two of these patients, who died at 13 and 22 years of age, died of rheumatic heart disease and kidney failure, respectively. The third patient, who had abandoned follow-up and was living on the streets, died at 22 years of age of dehydration caused by diarrhea of unknown etiology.

Five adolescents became pregnant during follow-up, giving birth to a total of 7 children, 5 of whom were girls. Five of these children who are now >18 months of age were tested serologically and tested HTLV-1 negative even though 1 was breast-fed for 6 months. At present, none has developed this skin disease. Four of the mothers were and continued to be in remission at latest follow-up; the fifth showed dramatic improvement during her pregnancy but experienced a relapse after giving birth.

Table 2. Frequency of Lesions in Infective Dermatitis Associated With Human T-Cell Lymphotropic Virus

Lesions	Patients, No. (%)
Erythematous-scaly-crusty lesions	42 (100)
Retroauricular fissures	32 (76.2)
Slightly erythematous-scaly papules	32 (76.1)
Crusting of nostrils	27 (64.3)
Fine papular rash	25 (59.5)
Blepharoconjunctivitis	24 (57.1)
Follicular papules	19 (45.2)

DISCUSSION

Apart from the cases reported in the state of Bahia, 2 other cases of IDH have been documented in detail in Brazil, one in Rio de Janeiro, the capital city of the state of Rio de Janeiro, and another in Campinas, a city in the state of São Paulo. In both cases, there were lesions on many areas of the body, including the scalp and retroauricular areas [17, 18]. One child had been breast-fed, and the mother had HAM/TSP [18]. It is possible that the majority of cases of IDH are found in Bahia, because this is one of the most endemic regions for HTLV-1 in Brazil [1]. However, in many states in Brazil, including Maranhão, there are no projects designed to evaluate IDH. The predominance of girls in this study was expected, because IDH has been reported to be more prevalent in female patients [8, 19]. The mean age at onset of the disease was 2.6 years; however, 42% of the patients were <18 months of age, a finding that

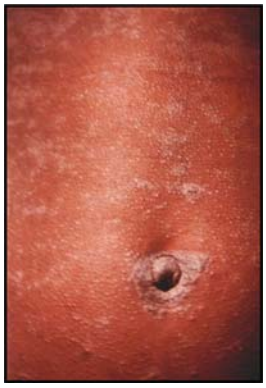

Figure 5. A 9-year-old female with disseminated erythematous-scaly papules and follicular papules since 8 years of age.

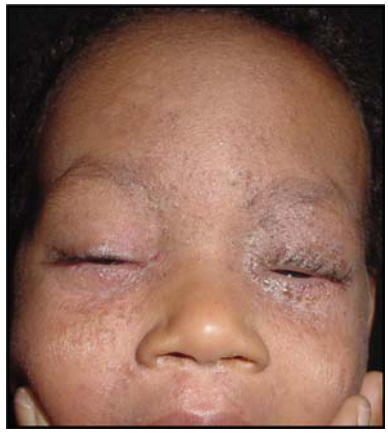

Figure 6. A 3-year-old male with IDH since 2 years of age. Bilateral blepharoconjunctivitis. The eyebrows are also involved.

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differs from data reported in the literature [4]. This earlier onset of IDH in this region has been reported elsewhere [9].

In this study, infection was probably acquired vertically, possibly as a result of prolonged breast-feeding, except in 1 child who had received a blood transfusion and whose mother was seronegative. The patients had been breast-fed for a median of 24.2 months. It has already been established that the frequency of vertical transmission is directly proportional to the time of breast-feeding, transmission rates being higher after 6 months of breast-feeding [20]. Of interest, in 4 cases transmission did not occur vertically because the patients' mothers were serologically negative. Transmission through breast-feeding cannot be completely ruled out, however, because the children had been breast-fed by other women. Cross-nursing is a relatively common habit among the poor in Brazil.

According to La Grenade et al [8], the areas affected in IDH are the scalp, axillae and groin, external ear and retroauricular areas, eyelid margins, paranasal skin, and/or the neck; however, no reference was made to the frequency of the affected areas. In the present case series, lesions were present on more areas of the body, being found on ≥3 areas of the body in all cases. Furthermore, the scalp and retroauricular areas were invariably affected, and lesions were disseminated in 83% of cases. The frequent finding of lesions in the antecubital and popliteal fossae may sometimes hamper differential diagnosis of atopic dermatitis.

The cases evaluated here fulfill the principal criteria for a diagnosis of IDH recently suggested in a review article [21]. Crusting of the nostrils was a common finding; however, this feature was absent in some patients, and in 2, it appeared only during subsequent relapses. Therefore, the presence of crusting of the nostrils cannot be considered an obligatory factor for the diagnosis of IDH, although it represents an important criterion for diagnosis when present. Because rhinorrhea is a common symptom in children in several other diseases, it should not constitute a criterion for diagnosis of IDH [21]. The relapsing nature of this disease was clear in all the patients, and in our opinion, this aspect should be considered to be indispensable for diagnosis. On the other hand, these findings suggest that the criterion requiring onset in early childhood should be removed, because the disease may begin later in childhood, as late as 11 years of age as shown in this study, or in adulthood [13, 14]. On the other hand, it is important to consider not only the serological diagnosis of HTLV-1 infection, which may fail, albeit infrequently, but also diagnosis of the infection by molecular biology. Two patients were serologically negative for HTLV-1; however, PCR for HTLV-1 was performed in PBMCs because of the presence of the classic characteristics of IDH, with this test ultimately confirming the presence of HTLV-1 infection.

In the literature, IDH is considered to disappear in adolescence; however, no information is available on the mean age or age range at which this occurs [22]. In the patients in the present study, the mean age at remission was 15 years (range, 10–20 years). It has also been shown that IDH may persist until at least 23 years of age. In 17 patients, IDH progressed to a definitive or probable diagnosis of HAM/TSP in childhood or adolescence, indicating a very high frequency (47.2%) of this association in Brazil and particularly in the state of Bahia. The prolonged follow-up was able to reveal a higher frequency of this association, compared with that previously registered at this center (30%) [10]. On the other hand, Araújo et al [23] reported that, of 5 adolescents with HAM/TSP reported in Rio de Janeiro, 3 also had IDH. However, these authors were addressing HAM/TSP in particular and failed to describe these cases of IDH in detail. In this respect, there appears to be a major difference between the disease in Brazil and that in Jamaica.

The association with scabies and xerosis found in the present study is also common in asymptomatic carriers of HTLV-1 and is not unique to IDH [21, 24]. As reported in the literature, *S. aureus* infection was present in the lesions in the great majority of cases [8].

In conclusion, the findings of the present study show that the most striking features of IDH and those that may be considered the most important for differential diagnosis are the prominence of the lesions, with fetid, yellowish crusting; the distribution of the lesions over a wider area, including the antecubital and popliteal fossae and various other areas; location of lesions on the scalp and retroauricular regions in 100% of cases; and the relapsing nature of the disease after discontinuation of treatment. In addition, in 36.8% of the patients, disease onset occurred very early, compared with other cases reported in the literature, at ≤12 months of age [4]. Furthermore, in serologically negative patients with typical IDH lesions, PCR testing should be performed in PBMCs. We suggest that, at least for cases identified in Brazil, the criteria shown in Table 3 should be applied. These criteria were modified from those defined by La Grenade et al [8] and already reported in a review article by 2 authors of the present article [21].

Table 3. Major Criteria for Diagnosis of Infective Dermatitis Associated With Human T-Cell Lymphotropic Virus

1. Presence of erythematous-scaly, exudative, and crusted lesions of the scalp, retroauricular areas, neck, axillae, groin, paranasal and perioral skin, ears, thorax, abdomen, and other sites
2. Crusting of nostrils
3. Chronic relapsing dermatitis with prompt response to appropriate therapy but prompt recurrence on discontinuation of antibiotics
4. Diagnosis of HTLV-1 infection (by serological or molecular biological testing)

Modified from La Grenade et al [8]. Of the 4 major criteria, 3 are required for diagnosis, with mandatory inclusion of 1, 3, and 4. To fulfill criteria 1, involvement of ≥3 of the sites is required, including involvement of the scalp and retroauricular areas. Abbreviation: HTLV-1, human T-cell lymphotropic virus type 1.

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Notes

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Potential conflicts of interest. All authors: No reported conflicts.

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