Abstract

Objectives: To review the literature on diseases linked with infection by human T-cell lymphotropic virus type I (HTLV-I) in childhood and adolescence, with focus on clinical aspects, diagnosis, pathogenesis, progression and treatment.

Sources: Medical literature published during the last 20 years identified using PubMed and MEDLINE and from specialized medical books, with emphasis on infective dermatitis associated with HTLV-I (IDH), on the juvenile form of HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP), on adult T-cell leukemia/lymphoma (ATL) and on HTLV-I-associated uveitis. Keywords used to search databases were: HTLV-I-associated infective dermatitis, HTLV-I-associated myelopathy/tropical spastic paraparesis, adult T-cell leukemia/lymphoma, HTLV-I-associated uveitis.

Summary of the findings: IDH is a chronic, relapsing and infected dermatitis of childhood which always involves the scalp and which may progress to HAM/TSP and ATL. HAM/TSP is a chronic and incapacitating myelopathy of adults. There are 17 well-documented cases of HAM/TSP in children and adolescents in the literature, 12 of whom are patients with IDH. In contrast with the adult form of the disease, the juvenile form is rapid and progressive. ATL is a type of T-cell leukemia/lymphoma that affects adults and is generally fatal. Eleven of the 24 published reports of ATL in children and adolescents were diagnosed in Brazil.

Conclusions: These diseases are likely to be more common in childhood and adolescence than the literature would suggest. It is advisable that serological testing be performed for HTLV-I in children and adolescents suffering from chronic and relapsing eczema, with signs and symptoms of myelopathy or with a diagnosis of T-cell leukemia/lymphoma. It is important that pediatricians know how to recognize the pediatric manifestations of this infection in order to correctly diagnose them and offer their patients appropriate guidance and treatment.

Frequency of infection by HTLV-I

Infection by HTLV-I is endemic in many parts of the world, including the southwestern Japan, Caribbean islands, Central and Western Africa, the southeastern United States and South America. In Salvador, Brazil, a frequency of 1.35% was observed among blood donors, whereas, in other Brazilian state capitals (Recife, Rio de Janeiro, Manaus and Florianópolis) infection rates varied from 0.3 to 0.8%. Nevertheless, a higher frequency has been recorded in Pará (1.6%). In Campo Grande (MS), an infection rate of 10% was observed among Japanese immigrants and their descendents, and, in Salvador (BA), a rate of 25% was observed among injecting drug users.

The overall prevalence of this infection in the general population of Salvador was estimated to be 1.76%.

An HTLV-I infection frequency of 1.1% was observed among pregnant women in Belo Horizonte (MG) and of 0.84% in Salvador (BA). An epidemiological survey of the infected pregnant women in Salvador suggested that their infections had primarily been acquired via breastfeeding and, in second place, sexually. In these women the infection did not interfere with the course of pregnancy, and 15.6% of them reported having had eczema when children, whereas, just 0.85% of a control group of HTLV-I-negative pregnant women had had eczema. This demonstrates that there is a close relationship, in Salvador, between childhood eczema and infection by HTLV-I.

Modes of transmission

Transmission of HTLV-I is by sexual contact, blood transfusion, vertical (from mother to child) or, in injecting drug users, through sharing contaminated needles. Sexual transmission is primarily from men to women, at a rate of around 61%, whereas transmission from women to men is uncommon, at around 0.4%.

The principal form of vertical transmission is via breastfeeding. Transmission via human milk is almost always vertical, but it may occur by means of breastfeeding by wet-nurses or cross-breastfeeding (horizontal transmission). The milk of mothers who are seropositive for HTLV-I contains infected cells and experimental infection has been achieved administering this milk orally to marmosets. In areas where HTLV-I is endemic, from 7 to 42% of breastfed children acquire the infection. It is also known that non-breastfed infants can also acquire the infection vertically, with a frequency that varies from 3.3 to 13.8%. In these cases, transmission is likely to be transplacental or from contamination in the birth canal.

Bittencourt et al., in 2002, used polymerase chain reaction (PCR) to assess 41 children who were born to carriers and who had not been breastfed (mean age of 11 months) and did not detect any cases of transmission. However, 81% of these mothers had undergone elective caesarian. This type of delivery reduces vertical infection rates of the acquired immunodeficiency virus (HIV) infection, and the possibility that it may also have interfered in the absence of vertical transmission in these cases cannot be ruled out.

Diagnosis of infection

Routine diagnosis of HTLV-I infection is serological, by means of serum assay for anti-HTLVI/II antibodies, the enzyme-linked immunosorbent assay (ELISA) being the most widely used. Diagnosis must be confirmed using western blot technique, which allows differentiation between the types I and II of the HTLV. It should be pointed out that a positive test before 1 year of age may not represent infection and may be merely the result of maternal antibodies passing through the placenta.

In cases that cannot be confirmed using the western blot technique, molecular testing should be carried out, the PCR being the most often used. Detection by PCR does not depend on antibody production because it directly detects the proviral DNA. As a result of its elevated sensitivity and specificity, this method is capable of shedding light on indeterminate serological status and even of detecting infections in seronegative individuals with clinical status suggestive of HTLV-I-associated diseases. This is also the method of choice for very early investigation of infection.

The principal diseases related to HTLV-I

In contrast with the majority of infected individuals who remain asymptomatic, in other patients HTLV-I can cause serious diseases, including ATL, HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP) and HTLV-I-associated infective dermatitis (IDH). IDH is a childhood disease; however, ATL and HAM/TSP are considered to represent adult diseases, as is HTLV-I-associated uveitis. Other diseases have been related to this virus in adulthood, such as lymphocytic T-cell alveolitis, Sjögren’s syndrome, thyroiditis, Behçet’s disease, arthropathy and polymyositis.

Infection by HTLV-I involves dysregulation of the immune system with spontaneous lymphoproliferation and simultaneous cytokine production by helper T-cells types I and II, which makes the infected individuals more susceptible to other infections and parasitoses, such as scabies and strongyloidiasis. It was recently observed in Salvador that HTLV-I carriers have a greater risk for tuberculosis than do individuals who are not infected with the virus.

Lack of knowledge of IDH, together with the belief that ATL, HAM/TSP and HTLV-I-associated uveitis are late-
onset diseases, may be responsible for the low number of HTLV-I-associated diseases diagnosed during childhood and adolescence. In the pediatric literature, these pathologies are scarcely found, and we believe it is quite important to underscore their occurrence.

**HTLV-I-associated infective dermatitis**

**Introduction**

IDH is a recurrent, infected form of eczema that was described in Jamaica in 1966 by Sweet, and which was later linked to HTLV-I. Onset is generally after 18 months of life and the disease rarely persists until adulthood. In these cases transmission is vertical. There is only one report of a case where transmission was via blood transfusion. The frequency of IDH is greater among females, varying from 60 to 65.

The greatest number of cases of IDH have been reported in Jamaica and, more recently, in Bahia. Smaller series of cases have been described in Trinidad and Tobago, Peru and Senegal. Curiously, in Japan, where the prevalence of HTLV-I infection is elevated, only two cases of children with IDH have been reported, both of which progressed to ATL in adulthood.

In Jamaica, IDH is responsible for 10% of childhood eczema cases. In that country the prevalence of HTLV-I is 1% in children, and 8.1% in individuals older than 20 years. Maloney et al. monitored 28 children with HTLV-I for an average of 7.5 years, observing that only one developed IDH. Based on this observation, they concluded that the probability of developing IDH by 4 years of age was 2% among the perinatally infected children.

**Clinico-pathological and immunohistochemical aspects**

The lesions in IDH are erythematous, scaly, and crusted. They involve the scalp, neck, ears (Figure 1), retroauricular areas, axillae, groin, genitalia (Figure 2) and several other parts of the body. The patients complain of itching that is less intense than that found in atopic dermatitis (AD). Patients also exhibit erythematous, scaly, and/or crusted lesions in the nostrils and/or rhinitis and, with frequency, blepharoconjunctivitis (Figure 3). The disease may become generalized and exhibit pustules, erythematous and scaly follicular papules (Figure 1), and retroauricular fissures. IDH is always associated with infection by *Staphylococcus aureus* and/or *Streptococcus β-hemolyticus*.

According to La Grenade et al., the principal diagnostic criteria for the diagnosis of IDH are: 1. Eczema of the scalp, axillae, groin and external ear, retroauricular regions, eyelids, paranasal skin and/or neck; 2. Chronic rhinorrea and/or crusted lesions at the nasal vestibule; 3. Chronic
relapsing dermatitis which responds immediately to antibiotic therapy and relapses immediately once treatment is withdrawn. 4. Early childhood onset. 5. HTLV-I seropositivity. These authors state that items one, two and five must be present and that at least two of the areas listed in item one must be involved for that criterion to be met. While these criteria consider crusting of the nostrils and/or rhinitis as compulsory elements for diagnosis, these features are not persistent and may be absent in some cases.27

In common with what is observed with adult infected by HTLV-I,20,22 complications of infectious or parasitic nature are also seen in patients with IDH, such as otitis, pyodermatitis, scabies and strongyloidiasis.27,31,36,37

Although it is not possible to diagnose IDH histopathologically, histology is still important for differential diagnosis from other inflammatory dermatoses and mycosis fungoides. Histological findings of IDH are those of spongiotic dermatitis or simple chronic dermatitis. Infrequently histology may mimic psoriasis or mycosis fungoides.38

In IDH, the inflammatory infiltrate is predominantly made up of CD8+ T-cells. In contrast with what is observed in AD and in seborrheic dermatitis (SD), CD8+ lymphocytes predominate over CD4+ lymphocytes. Nevertheless, the CD8+ lymphocytes are perforin negative and, rarely, granzyme-B+, indicating that they are not activated cytotoxic T-lymphocytes. In contrast, in AD, lymphocytes are perforin+ and granzyme-B+ and do appear to contribute to the inflammatory process.38

**Differential clinical diagnosis**

In IDH differential diagnosis should primarily aim to rule out AD and later, when the child enters puberty, SD. A positive serological test for HTLV-I is not the unique criterion to diagnose IDH in patients with chronic eczema in endemic areas, because cases of AD or SD may be seropositive in these areas.

The lesions observed in the childhood form of AD, which begin after 2 years of age, are similar to a certain extent to those observed in IDH; however, IDH lesions are more infected and exuberant. On the other hand, itching caused by IDH is less intense than that found in AD. Besides, in contrast to AD, in IDH crusting of the nasal vestibule, fissures, generalized rash with very small papules and blepharoconjunctivitis are observed.39,40 Childhood SD is considered as a rare entity, however Maloney et al.41 observed that 25% of children carrying HTLV-I had SD. The lesions in IDH, in contrast to the lesions found in SD, are more exsudative and fetid with yellowish crusts. In addition, the SD lesions present greasy scales.42 On the other hand, the *Pityrosporum* yeasts, which frequently occur in SD,43 are not observed in IDH lesions. Furthermore, IDH responds well to sulfamethoxazole/trimethoprim and to antibiotics, which is not a characteristic of SD.27

**Pathogenesis**

It is not known why only a few infected children developed IDH and the majority remain asymptomatic. It is possible that genetic factors in the host play an important role in the genesis of IDH. La Grenade et al.44 used human leukocyte antigen (HLA) genotyping to study three generations of one same family containing nine carriers and three cases of IDH, of whom a mother and one child later progressed to HAM/TSP. They observed that the mother and the child with IDH and one other child who was a carrier had a class II DRB1*DQB1* haplotype, which is the same that has been described among Japanese patients with HAM/TSP.

Some research has shown that patients with IDH have a higher viral load. According to La Grenade et al.,28 patients with AD who are infected by HTLV-I present lower serum anti-HTLV-I antibodies than patients with IDH. Considering that there is a positive correlation between the levels of anti-HTLV-I antibodies and the viral load,41,45 this finding appears to indicate that the viral load of IDH patients is more elevated than that of children who are only carriers. Recently, Maloney et al.,35 studying 28 infected children, observed that just two of them exhibited elevated viral load, and one of these developed IDH.

The marked cutaneous inflammatory involvement may be the result of cytokine action. It is known that the Tax viral protein can transactivate genes of several proinflammatory cytokines, including interleukin-1, interleukin-6 and tumor necrosis factor alpha (TNF-α). It is possible that these cytokines could amplify and maintain the cutaneous inflammatory reaction, which would also explain the recurrent nature of IDH.46 A study of the cytokine profile in IDH, evaluating the concentrations of IFN-γ and TNF-α in the supernatant of the peripheral blood mononuclear cells, demonstrated high levels of these cytokines compared with infected individuals who did not have IDH (Nascimento, personal communication).

**Clinical course and treatment**

IDH may progress to HAM/TSP47 and ATL.32,48,49 Forty-four percent of ATL cases diagnosed in Bahia have a history of severe eczema in childhood, resistant to treatment and with involvement of the scalp, undoubtedly IDH cases.50

It is, therefore, advisable that serology for HTLV-I be carried out in all cases of severe eczema in children and adolescents. Additionally, IDH cases should be monitored with periodic clinical and neurological examinations. Since strongyloidiasis is a predisposing cofactor for a progression
to ATL, leading to clonal expansion of lymphocytes, and considering that this parasitosis is frequently asymptomatic, it is important that it be searched routinely in all patients with IDH, since appropriate treatment can reverse clonal expansion.51

Since IDH is always associated with bacterial infection, it responds well to antibiotic therapy and oral trimethoprim/sulfamethoxazole. Nevertheless, when medication is withdrawn relapse occurs.27

**HAM/TSP in childhood and adolescence**

**Introduction**

HAM/TSP is a severe and incapacitating myelopathy, more common among females and with a mean age of onset of 46.52,53 It is generally considered to be the result of an infection acquired during adulthood through blood transfusion or sexual transmission.54

According to the guidelines of the World Health Organization (WHO), clinical manifestations and the presence of anti-HTLV-I antibodies in serum and cerebrospinal fluid are considered essential criteria for the diagnosis of HAM/TSP.47 Clinical status is compatible with chronic and progressive spastic paraparesis, primarily involving the pyramidal tract (lower limb hyperreflexia, clonus and Babinski reflex), with proximal weakness of lower limbs, neurogenic bladder and lumbago.47

During the evolution of HAM/TSP, invariably motor and/or sensory signs and symptoms related to symmetrical limited crural function are observed. These include fatigue when walking, resulting from progressive spasticity of the lower limbs, hyperreflexia, clonus, muscle weakness, and sensory complaints, such as lumbar pain, cramps, numbness and/or tingling with tactile dyesthesia of the feet.47,53 These signs and symptoms are present with different intensities throughout the several clinical phases of the disease.

In the differential diagnosis, it is important to rule out other infectious diseases which can compromise the spinal cord, such as syphilis, toxoplasmosis, cystercercosis and schistosomiasis, by testing for antibodies in cerebrospinal fluid and culturing for other microorganisms, including *Mycobacterium tuberculosis*.47

Depending on disease duration and on the number of cells present in the cerebrospinal fluid (CSF), HAM/TSP cases are classified as acute, subacute or chronic.53 When evaluating progress, it is important to apply Osame's motor incapacity scales and the Kurtzke expanded scales, with the aim of measuring the degree of incapacity of the various functional systems, in addition to controlling progression and the response to different treatment attempts.47

Although HAM/TSP is considered a pathology of adults, there are 17 well-documented cases in the literature of HAM/TSP diagnosed in children and adolescents, 13 of which were described in Brazil.47,49,55-61 In these cases a predominance of the female sex was observed. In contrast with the adult form of the disease, in the juvenile form of HAM/TSP infection is acquired vertically.47,62

**Clinical status, diagnosis and progression**

The great majority of cases of HAM/TSP in children and adolescents occurred in patients with IDH or who have had IDH.63 In a study that carried out neurological assessment of 20 IDH patients in Salvador, it was observed that only eight patients (40%) exhibited no neurological manifestations. In six cases (30%), a conclusive diagnosis of HAM/TSP was made; four patients (20%) manifested fluctuating myelopathy symptoms;63 and one of them received the same diagnosis later (Primo, unpublished data). Furthermore, two other cases (10%) exhibited clinical manifestations suggestive of peripheral neuropathy.63 This pathology has been described in adults with asymptomatic infection or with HAM/TSP.64

Vesical dysfunction, characterized by difficulty in emptying the bladder, urinary urgency and incontinence, that is observed in adult HAM/TSP65,66 are also found in the juvenile form of the disease.47 Considering that bladder involvement may go unnoticed, urodynamic studies are important for diagnosis, and are also useful for treatment and follow-up of vesical dysfunction. Urodynamic studies carried out for three juvenile cases of HAM/TSP revealed similar features to those observed in adults.67

There are reports of short stature, hypocalcemia, and small increases in urinary phosphorus excretion and of cyclic adenosine monophosphate (AMP) after injection of parathyroid hormone (HPT) in juvenile HAM/TSP, findings which led to the diagnosis of pseudohypoparathyroidism (PHP).68 According to Machigashira et al.,69 HTLV-I infection does not induce PHP, but PHP may be a risk factor for the development of HAM/TSP in carriers of the virus. This aspect should be investigated more extensively.

Although the juvenile form of HAM/TSP exhibits similar clinical manifestations to the adult form, its clinical course is different, being rapidly progressive.47,58

**Pathogenesis**

Recently, a clustering of HAM/TSP cases was observed in three families, between siblings or between mother and child,47 which suggests that genetic factors are involved in the genesis of this pathology. In Japan, it was observed that adult HAM/TSP had a different immunogenetic background from ATL.70

Patients with IDH and HAM/TSP exhibit high levels of anti-HTLV-I antibodies.47 Considering that there is a correlation between the levels of antibodies and the
that vertical transmission, the latent period before its
Notwithstanding the fact that ATL is generally related to
lymphoma that is etiologically linked with HTLV-I.

Introduction

Adult T-cell leukemia/lymphoma

Introduction

ATL is a severe and generally fatal form of leukemia/lymphoma that is etiologically linked with HTLV-I. Notwithstanding the fact that ATL is generally related to vertical transmission, the latent period before its development is very long. In Brazil, many cases of ATL have been detected, the mean age varying from 42 to 49 years, which is a decade younger than in ATL cases in Japan.

As has already been mentioned, it has been observed that Strongyloides stercoralis stimulates oligoclonal proliferation of cells infected with HTLV-I in asymptomatic carriers, suggesting that this infestation may be a cofactor for the development of ATL. It is probable that the earlier onset of ATL in developing countries where the prevalence of Strongyloides stercoralis infestation is higher, is at least in part the result of a greater exposure of HTLV-I carriers to this parasite.

There are 24 published reports of ATL diagnosed in childhood or adolescence (Table 1). The clinical manifestations of these cases are, in the majority, similar to those observed in adults. Six cases were younger than 11 years of age at the time of diagnosis.

Maternal serology was positive in 16 of the 19 cases of the literature where this information was available, indicating vertical transmission of HTLV-I. Notwithstanding, serology was negative in three mothers. In one child, transmission occurred via blood transfusion. The other two children had been breastfed by another woman, whose serological status was unknown.

Clinical aspects

ATL is classified according to clinical and laboratory data, into smoldering, acute, chronic and lymphoma. The majority of the cases reported in the literature do not mention the clinical form; however, considering the clinical and laboratory data, the majority were in the acute form of ATL. Two cases were considered as chronic and three as smoldering, while two others exhibited the characteristics of this last clinical form. The organs most often involved were skin, lymph nodes, liver and spleen. Bone marrow was infiltrated in 10 of the 16 cases that made this examination. Macular rash, papules, infiltrated plaques, nodules, tumors or erythroderma were described in the skin, not differing from what is observed in adults. In three cases there was an association with IDH, and in another, history was highly suggestive of this dermatosis.

Diagnosis

The diagnosis of the patients was hematological and/or histopathological. In eight cases, monoclonal HTLV-I integration was observed (Weyenberg & Farré, unpublished data).

In only few cases of the literature the lymphomas were classified according to the histological type. They found pleomorphic lymphomas (currently defined as nonspecific peripheral T-lymphomas), mycosis fungoides and anaplastic large-cell lymphomas. These types of lymphoma have also been described in adult ATL.

Evolution

In the 15 cases with death, the survival was less than 6 months. In eight cases in which death was not recorded,
survival varied from 1.3 to 14 years. Three cases were considered as smoldering form, which presents a better survival, and two had the clinicopathological characteristics of this form of ATL.76 The clinical course of case 14 was abnormal. Lesions emerged at 7 years age and, at 24 years old, the patient’s lesions remain restricted to the skin, although their number and size have progressively increased, making electron radiotherapy necessary to reduce them. (Bittencourt, unpublished data).

Two univitelline twins behaved differently after infection by blood transfusion soon after birth.88 One developed ATL, with cutaneous lesions from 5 years onwards, while the other remained infected and asymptomatic at least until 13 years of age. Nevertheless, there is a report of two siblings who developed lymphoma early, one at 16 years and the other at 24 years of age.94 This report demonstrates a familial tendency in the development of ATL, which has already been observed in adult patients.94

Pathogenesis

IDH cases can progress to ATL, but the mechanisms that lead to this development have not yet been elucidated. It is probable that both genetic factors of the host and external factors are involved. On the other hand, there are many cases of ATL that have no history of IDH.

In IDH, the presence of viral antigens and bacterial superantigens may stimulate the lymphocytes and, therefore, an increased number of target cells available to be infected by HTLV-I. Along with this expansion of the infected T-cells, activation signals and growth factors would be produced for uninfected T-cells, and repeated clonal expansions of these cells would then increase the chances of the additional events required for transformation and leukemogenesis.46

Gabet et al.51 studied the HTLV-I replication over 2 years in a patient with IDH associated with strongyloidiasis, a parasitosis which predisposes carriers of the virus to develop ATL.75 They observed elevated viral loads, together with persistent oligoclonal expansion of infected lymphocytes. The replication pattern was very different from that observed in asymptomatic carriers, being more similar to the pattern found in ATL.51

In animal experiments, inoculation of HTLV-I via the oral route induces host HTLV-I-specific T-cell unresponsiveness and results in increased viral load. Since there are similarities between experimental oral inoculation and infection by breast-feeding, these findings

Table 1 - Cases of ATL in childhood and adolescence76

<table>
<thead>
<tr>
<th>No.</th>
<th>Authors</th>
<th>Age/sex</th>
<th>Skin</th>
<th>LN</th>
<th>Spleen and/or liver</th>
<th>BM</th>
<th>CNS</th>
<th>Survival (years)</th>
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<td>1</td>
<td>Vilmer et al.77</td>
<td>1/M</td>
<td>+</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>2</td>
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<td>16/F</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<td>10/F</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
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<td>7/F</td>
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<td>-</td>
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<td>17/M</td>
<td>-</td>
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<td>12/M</td>
<td>-</td>
<td>...</td>
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<td>Wilks et al.84</td>
<td>16/F</td>
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<td>16/F</td>
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<td>-</td>
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</tr>
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<td>Lin et al.86</td>
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<td>+</td>
<td>-</td>
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<td>13/M</td>
<td>+</td>
<td>-</td>
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<td>+</td>
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<td>Bittencourt et al.89</td>
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<td>+</td>
<td>-</td>
<td>Death (1.9)</td>
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<td>+</td>
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<td>-</td>
<td>Alive (14)</td>
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<td>+</td>
<td>-</td>
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<td>18/M</td>
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<td>+</td>
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<td>...</td>
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</tr>
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<td>11/M</td>
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<td>...</td>
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<td>+</td>
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<td>-</td>
<td>Death (0.2)</td>
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<td>16/F</td>
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<td>7/M</td>
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<tr>
<td>23</td>
<td>Mahé et al.31</td>
<td>17/F</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>...</td>
<td>-</td>
<td>Death (0.16)</td>
</tr>
<tr>
<td>24</td>
<td>Oliveira et al.91</td>
<td>16/F</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Alive (1.4)</td>
</tr>
</tbody>
</table>

ATL = adult T-cell leukemia/lymphoma; BM = bone marrow; CNS= central nervous system; LN = lymph nodes; ... = not reported.
* Monoclonal viral integration.
† Bone marrow involved in four cases.
strongly suggest that the known epidemiological risk factors for ATL (vertical transmission and high viral load) are linked by an insufficient specific T-cell response. This risk might be reduced if the carrier recovers the specific immune response.\(^95\) Thus, there would be an elevated risk for development of ATL in a small group of vertically infected carriers with a persistently low immune response to the virus, despite the presence of an elevated viral load. It is probable that the magnitude of the host immune response at primary infection might be a crucial determinant of persistent HTLV-I levels.\(^95\)

It is possible that the development of ATL during childhood or adolescence could be related to acquisition of the infection very early, by intrauterine transmission, in the birth canal or via breastfeeding in the first months of life, considering that the immune system of the fetus and child during the first few months of life is much less efficient.

### Treatment

It is very important that ATL cases are recognized, since both prognosis and treatment are different from the other types of leukemia/lymphoma. ATL does not respond to chemotherapy as do other lymphomas and leukemias and, within a variety of treatment protocols that are being tried out, the most widely used is interferon-alpha in association with zidovudine.\(^96,97\) It is important to emphasize that therapeutic management also depends on the clinical form of ATL.\(^96,97\)

### Ocular manifestations

Opacity and ulcer of the cornea have been described in IDH patients.\(^27,36\)

HTLV-I-associated uveitis is a disease of middle-aged adults which can occur in HTLV-I carriers, or in patients with HAM/TSP.\(^98\) Notwithstanding, there are five reported cases of HTLV-I-associated uveitis in children aged from 3 to 14 years; four of them were female, and with cases of HTLV-I-associated uveitis in children aged from 3 to 14 years; four of them were female, and with abnormalities in three adolescents with HTLV-I, stating that the lesions of these cases differed from vascular abnormalities commonly seen in HTLV-I-associated uveitis. Progression is slow, response to corticosteroids is poor and the final result is diffuse chorioretinal degeneration.

### Conclusions

As has been stated, IDH, ATL and the juvenile forms of HAM/TSP occur in individuals who have been infected vertically, and it is known that the main route of vertical transmission is breastfeeding. This demonstrates the importance of preventing this form of transmission in endemic areas, such as Salvador, which should be based on serological screening of pregnant women, and counseling the seropositive mothers to avoid breastfeeding.\(^4\) Considering that the mothers infected with HTLV-I in our country are generally from lower social classes, it is necessary that alternative nutritional sources and pediatric care be provided for their children. In Nagasaki (Japan), a wide ranging intervention employing this strategy blocked around 80% of vertical HTLV-I transmission.\(^14\)

Vertical HTLV-I transmission poses a serious public health problem and merits more extensive investigation so that its significance in other Brazilian cities can be evaluated.

### References
