Review Article

# HUMAN T-CELL LYMPHOTROPIC VIRUS TYPE 1 (HTLV-1): WHEN TO SUSPECT INFECTION?

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**ABSTRACT**

Human T-cell lymphotropic virus (HTLV) infections have occurred for thousands of years. However, knowledge about their pathogenesis is recent. The virus is endemic in several regions around the world. In Brazil, it is present in all states at varying prevalence rates and it has been estimated that around 2.5 million Brazilians are infected. Genetic and immunological parameters of the host are the most important determinants of the clinical manifestations associated with infection. These can be divided into three categories: neoplastic, inflammatory and infectious. HTLV-associated myelopathy (HAM/TSP) and adult T-cell leukemia/lymphoma (ATLL) were the first diseases to be related to this retrovirus. More recently, countless other diseases have been correlated with the virus. The objective of this review is to provide an update on epidemiological, pathophysiologic, therapeutic and, primarily, diagnostic knowledge about HTLV, in order to encourage etiologic suspicion of HTLV in all its diverse clinical manifestations, which are currently rarely associated with this agent.

Key words: HTLV-I infection. HTLV-II infection. Tropical spastic paraparesis.

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## Introduction

The human T-cell lymphotropic virus type 1 (HTLV-1) was described in 1980 as the first human retrovirus, isolated from a patient with cutaneous T-cell lymphoma.[1] The HTLV-1 virus is endemic in several regions of the world, such as the South of Japan, the Caribbean, Africa, South America and the Melanesian islands. In Brazil, the virus has been detected in every state in which it has been investigated, with varying prevalence rates. It is estimated that approximately 2.5 million Brazilians are infected. The HTLV-2 virus is also present, and its prevalence is significant among indigenous Brazilian populations.[2] The majority of carriers remain asymptomatic throughout life. Genetic and immunological factors in the host are the principal determinants of the emergence of associated diseases.[3] In 1985, Gessain et al.,[4] demonstrated that patients with tropical spastic paraparesis (TSP) in Martinique, had positive serology for HTLV-1 in 68% of cases. In 1986, a similar neurological condition was described in Japan and named HTLV-I associated myelopathy (HAM).[5] Later, Román and Osame[6] (1988) concluded that they were dealing with the same disease, and the term HTLV associated myelopathy / tropical spastic paraparesis (HAM/TSP) came to be used. Since then, countless other diseases have been correlated with this infection: uveitis, Sjögren's syndrome, infectious dermatitis, polymyositis, arthropathies, thyroiditis, polyneuropathies, lymphocytic alveolitis,[7,8] cutaneous T-cell lymphoma, strongyloidiasis, scabies, Hansen's disease and tuberculosis.[3,9] Knowledge of the possible clinical manifestations of the HTLV virus has now become important in several different medical specialties. Therefore, the objective of this article was to present a systematic description of diagnostic suspicion, diagnostic criteria, treatment and guidance on transmission and prevention.

### Methodology

The first stage of the selection process for articles on HTLV infection and its clinical manifestations comprised electronic searches on the MedLine, LILACS, ADOLEC and Cochrane Library databases. The keywords (DeCS/Mesh) used, alone and in combination, were: "HTLV-I Infections"; "HTLV-II Infections"; "Human T-lymphotropic virus 1"; "Human T-lymphotropic virus 2" "Nervous System Diseases"; "Paraparesis, Tropical Spastic";

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**Epidemiology**

The exact number of people infected by HTLV worldwide is unknown. It is estimated that 15 to 20 million people are infected, the majority with HTLV-1, and distribution is heterogeneous in different regions. High prevalence rates in the general population are observed in the South of Japan (10%), in Jamaica and Trinidad and Tobago (6%), Guinea-Bissau, Cameroon and Benin (5%).[9,10] In South America (Argentina, Brazil, Colombia and Peru) a 2% prevalence of seropositivity was observed among blood donors.[11] In Brazil, a study conducted with blood donors in the country's 27 capital cities, demonstrated a heterogeneous distribution, with a variation of 0.4/1000 in Florianópolis, SC, to 10/1000 in São Luís, MA. The states with the highest prevalence rates were Maranhão, Pará, Pernambuco and Bahia (6.7-10/1000). States with intermediate prevalence rates were Acre, Amazonas, Ceará, the Distrito Federal, Goiás, Minas Gerais, Paraíba, Rio de Janeiro and Tocantins (3.4-6.6/1000). All other states had prevalence rates below 3.4/1000.[12] It is known that the population of blood donors does not reflect prevalence in the general population, but underestimates it. In absolute terms, Brazil may have the largest number of seropositive people in the world.[12] In non-endemic areas, certain groups should be considered as at risk, such as immigrants from endemic areas, the sexual partners and descendents of people known to be infected, sex professionals and drug users.[9]

**Transmission**

The HTLV-1 and 2 viruses are present as proviruses, which are virus genomes that have integrated themselves into the DNA of the host's lymphocytes. Transmission can occur via transfusions, contaminated blood cell products are given. Between 20% and 63% of those infected are infected in this way.[13] Transmission between sexual partners is more common from the male partner to the female (the 10-year risk is 61%) and much rarer in the other direction (the 10-year risk is 0.4%).[13]

Transmission via breastfeeding is the result of contaminated lymphocytes in the milk, which are passed to the child. The risk of transmission increases as breastfeeding duration is prolonged (the probability is from 18% to 30%), becoming elevated with mixed breastfeeding. Maternal histories of transfusions, HAM/TSP or strongyloidiasis were associated with increased risk of transmission via breastfeeding. Vertical transmission is also possible via other routes, probably intrauterine or perinatal, although it is less common (4% to 14%).[13] Adding serology for HTLV to prenatal management is of fundamental importance to improving control of transmission via this route. Another known route of transmission is needle-sharing between intravenous drug users.[9,14] Transmission via organ transplantation has been described and is associated with rapidly progressing HAM/TSP, possibly because of the immunosuppression that transplant patients undergo.[9,15]

**Pathophysiology**

The majority of those infected by HTLV remain asymptomatic. People who do exhibit signs or symptoms are exposed to the infection for long periods before it manifests. A number of different factors are involved in the virus/host interaction and in transition from the asymptomatic state to the emergence of a disease associated with HTLV-1.[16] The relationship between HTLV-2 and neurological and systemic diseases is less well defined, although it appears that it is less frequent and less severe.[17-20] Syndromes that are part of the neurological complex related to HTLV-1 have a distinct pathogenic substrate from adult T-cell leukemia/lymphoma (ATL).[2] It is also not entirely clear how HTLV resists a competent immune system or what determines risk of development of the diseases associated with it. HAM/TSP is an immunomediated disease,[21] related to the host's immunoresponse to infection. The immunoresponse that attempts to control the infectious agent itself damages the nerve tissues, because of an exaggerated proinflammatory response. Elevated proviral load is the most evident risk factor for transition from the asymptomatic carrier status to myelopathy and immunomediated diseases. Additionally, there are certain HLA alleles in the host which are active in modulation of immunoresponse and confer a factor of susceptibility or protection. In ATL, HTLV expresses the oncogenic capacity of the viral genes, primarily Tax and HBZ, which alter the expression of cellular genes involved in control of cell replication and apoptosis.[16,22]

**Serological and laboratorial diagnosis**

Initially, lower-cost screening tests such as enzymatic immunoassay or agglutination tests are used. The low specificity of these tests means they often give false-positive results. It is recommended that positive results be confirmed by indirect immunofluorescence or Western Blot. These tests help to discriminate between HTLV-1 and 2, but may also return inconclusive results, making PCR (polymerase chain reaction) necessary to confirm diagnosis. Inconclusive results followed by negative PCR may suggest exposure to HTLV and merit monitoring.[23] Atypical lymphocytes (Flower Cells) may be observed in peripheral blood, as may hypergammaglobulinemia, and false-positive syphilis test results are also possible.[21]

**Neurological manifestations**

HTLV-associated myelopathy is the most classical neurological manifestation. It is characterized by spastic paraparesis with the proximal muscles of the lower limbs being the worst affected. The disease commonly manifests asymmetrically[24] and in conjunction with signs of pyramidal liberation: hyperreflexia, clonus and Babinski reflex. In general, clinical course is slow and progressive, affecting from 1% to 5% of infected people, with greater frequency among women. Patients are generally diagnosed between twenty and forty years of age.[25] Rapid progression, defined as incapacity and loss of the ability

to walk within 2 years of onset of symptoms, has been observed in some studies.[26] Table 1 lists the principal signs and symptoms observed in HAM/TSP and associated systemic manifestations that have been reported from cohort studies. It is possible that both peripheral nervous system and neuromuscular damage may be present in conjunction in HAM/TSP, but this can often be masked by the signs and symptoms resulting from damage to the central nervous system, which are more obvious during physical examination. Electroneuromyographic findings suggestive of polyneuropathy are observed in around 50% of HAM/TSP patients, while clinical signs and symptoms are observed in just 15% of them. Even when HAM/TSP is absent, peripheral damage may still be present and may affect people from the same family, deflecting diagnostic suspicion onto other etiologies.[28,29] Cases that mimic amyotrophic lateral sclerosis (ALS) have been described with clinical presentation and electroneuromyographic findings very similar to those found in seronegative patients. It should be pointed out that there are also signs and symptoms that are not normally observed in ALS, such as early sphincter dysfunction, abnormal vibration sensitivity, a possibility of responding to corticoid therapy and slower clinical progression.[28,30,31] Dysautonomia, clinically manifest as postural hypotension, arterial hypertension, changes in cardiac variability rates, impotence and urinary control dysfunction have been observed in patients with and without HAM/TSP.[32] Cognitive involvement has been studied very little to date. Slowed psychomotor functions, attention deficit and impaired visual-spatial abilities have been reported.[21] If neurological damage due to HTLV is suspected, investigations should be systematic and based on the clinical syndrome presented. In the presence of medullary syndrome, magnetic resonance should be requested for the whole medullary canal and a cerebrospinal fluid sample should be analyzed for cytometry, cytology, proteins and anti-HTLV antibodies assay. In peripheral

**Table 1 - Signs and symptoms observed in HAM/TSP and associated systemic manifestations**

| Author/Publication Date | CAROD-ARTAL et al., 2007[25] | GOTUZZO et al., 2004[26] | MILAGRES et al., 2002[27] |
|---|---|---|---|
| Number of HAM/TSP cases | 42 | 165 | 86 |
| Females | 26 (62%) | 120 (73%) | 52 (60.5%) |
| Mean age | 49.8 (years) | 51.5 (±12.4 years) | 49.4 (25-74 years) |
| Mean age at onset of symptoms | NP | 45.3 (±12.6 years) | 43.2 (11-64 years) |
| Mean time since onset | 11.2 (years) | NP | 6.2 (1-28 years) |
| Urinary incontinence | 28 (66.7%) | 123 (82%)* | 58 (67.4%) |
| Lumbar pain | 24 (57.1%) | 113 (79%) | NP |
| Paraparesia/spasticity | 42 (100%) | 152 (98.7%) | 82 (95.3%) |
| Hyperreflexia | 41 (97.7%) | 145 (95.4%) | 83 (96.5%) |
| Babinski reflex | 40 (95.2%) | 137 (92.6%) | 76 (88.4%) |
| Distal hypopallesthesia | 33 (78.6%) | 72 (61.5%) | NP |
| Sensitive lower limb symptoms | 21 (50%) | 111 (90.2%) | 70 (81.4%) |

*Nonspecific urinary complaints; NP: not provided.

neuropathy and myopathy, electroneuromyography of all four limbs should be requested. Serum creatine phosphokinase (CPK) should be tested if there is a suspicion of myopathy. For autonomic syndrome, clinical maneuvers can be used to assess postural hypotension, or alternatively the tilt-table test, in addition to ultrasound of the urinary system and a urodynamic study.[33] A team of specialists have developed diagnostic criteria for classifying HAM/TSP as definite, probable or possible.[34] Diagnosis of neurological diseases associated with HTLV starts from an initial diagnosis of HTLV infection, confirmed by serological and/or molecular methods in peripheral blood, combined with the presence of one or more of the neurological syndromes mentioned so far and after differential diagnosis with other causes of myelopathy: compressive processes (tumoral, spondylotic), deficiencies (vitamin B12 and folate), toxicity (alcoholism), vascular/metabolic causes (*Diabetes mellitus*, uremia and thyroid dysfunctions), autoimmunity (multiple sclerosis, connective tissue diseases, paraneoplastic conditions and others), infections and parasites (syphilis, HIV, schistosomiasis) and hereditary (adrenomyeloneuropathies, hereditary spastic paraparesis, Charcot-Marie-Tooth disease and others).[34] The most common findings in cerebrospinal fluid are discrete lymphocytic pleocytosis ($\leq$ 50 cells/mm$^3$) and mildly to moderately elevated protein, observed in around one half of patients. Oligoclonal bands can be found in cerebrospinal fluid and sometimes also in serum. Anti-HTLV antibodies are present in cerebrospinal fluid and titers are heightened in HAM/TSP.[9] Lezin et al.[35] proposed using the proviral cerebrospinal fluid load as a diagnostic criterion for HAM/TSP when greater than 10% and at a ratio or more than 1 to the load in blood. Magnetic resonance imaging reveals nonspecific lesions of periventricular and subcortical cerebral white matter in 50% to 80% of HAM/TSP

patients.[36] Spinal marrow MRI is abnormal in 14% of the patients with HAM/TSP with the principal finding being medullary atrophy of the thoracic segment. Abnormal signals, contrast enhancement and edema, when observed, are more common in the posterior or lateral spine, in the thoracic or cervical areas. Active inflammatory processes are associated with more rapid progression of the clinical course.[37] Imaging exams are of great importance in differential diagnosis, however, normal imaging results do not rule out HAM/TSP or other neurological damage relate to HTLV. There is no consensus in the literature on an effective specific treatment for the neurological manifestations of HTLV.[9] Symptomatic treatment is still the main method of minimizing the disorders associated with neurological damage (Table 2). Physiotherapy for motor and urinary dysfunction is very important.

**Adult T-cell leukemia/lymphoma (ATL)**

Adult T-cell leukemia/lymphoma (ATL) is caused by HTLV-1. The probability that infected people will develop ATL is 4%. In Japan, this occurs in 6% of infected men and 2% of infected women. There is a prolonged latency period between infection and the appearance of ATL, which is as much as 60 years in Japan and 40 years in Jamaica.[22] Table 3 lists the four major classifications of ATL.[38,39] The leukemic phase of ATL tends to spare the bone marrow; accentuated anemia and thrombocytopenia are not observed. White blood cell counts are always elevated and can be as high as 100,000/mm$^3$. Heightened leukocyte counts and elevated lactate dehydrogenase (DHL) and calcium levels are markers of worse prognosis. Atypical lymphocytes that are pleomorphic and lobulated and have significant nuclear abnormalities (flower cells) are found in peripheral blood. If left untreated it is rapidly fatal, with death caused by pulmonary complications, opportunistic infections, sepsis and uncontrolled hypercalcemia. The chronic and indolent forms of ATL are less common, but after a number of years they will evolve into the acute form.[40] Treatment of the indolent and chronic forms can be postponed until they evolve into the acute form; despite a less aggressive clinical course, prognosis for survival over the long term is poor. Some studies, with small patient samples and short follow-up periods, have demonstrated a satisfactory response and moderate toxicity using zidovudine in combination with interferon alpha, and both of these in combination with arsenic.[41] In the more aggressive acute and lymphomatous forms treatment should be started as early as possible using, CHOP chemotherapy regimens (cyclophosphamide, doxorubicin , vincristine and prednisolone). More powerful regimens such as VCAP (vincristine, cyclophosphamide, doxorubicin and prednisolone) or AMP (doxorubicin, ranimustine and prednisolone), offer a better response and prognosis, but mortality is higher. Treatment options described in the literature include: allogeneic stem cell transplant, inhibition of the *NF-kappa Beta* protein and monoclonal antibodies.[22]

**Table 2 - Symptomatic treatment of neurological manifestations**

| Symptoms | Drug/ Treatment | Dose/ Frequency | Most common side effects |
|---|---|---|---|
| Spasticity | Baclofen* | 10-80 mg/day | Somnolence |
| | Tizanidine* | 4-16 mg/day | Somnolence |
| | Diazepam* | 5-40 mg/day | Somnolence |
| | Botulinum toxin** | Individual | Weakness /Hypotonia |
| Bladder Neurogenic | Intermittent catheterization | 4/4 hours | Urinary tract infection |
| | | 6/6 hours | Urinary tract infection |
| | Oxybutynin | 5-15 mg/day | Dry mouth /Constipation |
| | Imipramine | 10-75 mg/day | Dry mouth/Constipation |
| Recurrent urinary infections | Nitrofurantoin | 100 mg/day | Nausea, vomiting |
| | Norfloxacin | 400 mg/day | Nausea, vomiting |
| Intestinal constipation | Nutritional guidance | Diet rich in fibers, hydration, physical activity | |
| | Psyllium mucilloid | 5.8-17.4 mg/day | Colic, diarrhea |
| | Mineral oil | 7.5-30 ml/day | Colic, diarrhea |
| | Lactulose | 10-30 ml/day | Colic, diarrhea |
| Neuropathic pain (Medullary, radicular or peripheral neuropathy-induced) | Amitriptyline | 25-150 mg/day | Somnolence/Constipation |
| | Nortriptyline | 25-150 mg/day | Constipation/Dry mouth |
| | Imipramine | 25-150 mg/day | Constipation/Dry mouth |
| | Gabapentin | 900-1800 mg/day | Somnolence |
| | Carbamazepine | 400-1200 mg/day | Ataxia, aplasia |
| | Oxcarbazepine | 600-1800 mg/day | Hyponatremia |
| | Phenytoin | 200-300 mg/day | Ataxia |
| | Duloxetine | 60-120 mg/day | Nausea |
| | Pregabalin | 150-300 mg/day | Dizziness/somnolence |

Adapted from: Castro-Costa CM, Araújo AQ, Menna-Barreto M, Penalva-de-Oliveira AC, 2005.[33] * It may be necessary to combine drugs to potentialize the therapeutic effects. ** Primarily administered to the adductor musculature of the thigh.

**Table 3 - Forms of clinical presentation of adult T-cell leukemia/lymphoma**

| ATL TYPE | CLINICAL PRESENTATION |
|---|---|
| Indolent | Normal white blood count, with less than 3% atypical lymphocytes. Limited to cutaneous lesions. |
| Chronic | Lymphocytosis, lesions of skin, liver and lungs and lymphadenopathy. |
| Lymphomatous (10 to 15%) | Non-Hodgkin's T cell Lymphoma, without blood or bone marrow involvement. Normal white blood count, with 1% or less of atypical lymphocytes. Cutaneous damage and lymphadenopathy predominate. Primary central nervous system damage may be present. |
| Leukemic (75%) | T-cell leukemia, with hypercalcemia, osteolytic lesions, lymphadenopathy, visceral involvement or leptomeningeal and opportunistic infections. |

Adapted from: Ratner L, 2005;[38] Lopes MSSN, Dobbin JA, 2006.[39]

**Polymyositis, inclusion body myositis and fibromyalgia**

Polymyositis and inclusion body myositis are described in association with retrovirus infections (HIV and HTLV). Neither the diseases themselves nor muscle biopsy findings differ from the presentation observed in uninfected patients. Myopathy can affect patients irrespective of the presence of other neurological manifestations. In one region of Japan, between 1986 and 2006, Matsuura et al.[42] observed higher prevalence rates for the combination of inclusion body myositis and HTLV (11 out of 21 patients, 52.3%), than for polymyositis (27.5%), with a seropositivity rate of 11.6% in the general population. They identified a high proviral load and immune susceptibility as the principal factors in emergence of the pathological process. Response to immunosuppressor treatment was considered unsatisfactory, emphasizing these entities' possible association with HTLV infection. An association has been demonstrated between fibromyalgia and chronic viral infections. Cruz et al.[43] found fibromyalgia in 38% of people infected with HTLV and in 4.8% of controls, demonstrating a significant association (OR 9.14, 95% CI 2.42-34.52).

**Erectile dysfunction and urinary symptoms**

Urological urinary and sexual manifestations may signal an initial stage of HAM/TSP. During the initial phases the most common urinary symptoms are nocturia, urge urinary incontinence and dysuria, progressing to feelings of micturition effort, incomplete bladder emptying and incontinence.[44,45,46] Erectile dysfunction is reported in 88.2% of patients with HAM/TSP, in comparison with a rate of 17% in the general population.[44] Rocha et al.[47] observed symptoms suggestive of urinary infection in HTLV carriers, but did not confirm infection by urine culture in the majority of cases (81%). Urodynamic studies showed signs of neurogenic bladder and detrusor hyperreflexia in the great majority, followed by dyssynergy of detrusor muscle and external sphincter. Neurogenic bladder is an important early sign of myelopathy and these patients should *not* be given empirical treatment for urinary infection. In a study conducted by Castro et al.,[48] 63 (80.8%) out of a total of 78 patients with the HTLV virus had abnormal urodynamic findings including detrusor muscle hyperactivity (52.4%) and dyssynergy of detrusor muscle and external sphincter (25.4%). Patients with HAM/TSP primarily exhibited the second of these conditions (p=0.005; OR=5.5;CI 1.6 to 19.4)

**Ophthalmological, lacrimal and salivary glands involvement**

Giozza et al.[49] observed "dry syndrome" in 75% of patients with HAM/TSP and in 22% of HTLV carriers free from neurological damage. They stressed that the pathophysiologic mechanisms were different from those observed in Gougerot-Sjögren Syndrome since anti-SSA and anti-SSB immunological markers were absent, suggesting patterns of involvement similar to those observed in HIV and hepatitis C infections. Pinheiro et al.[50] observed dry keratoconjunctivitis in 54.5% of HAM/TSP patients, in 20.3% of asymptomatic carriers and in 12.7% of healthy controls. Soares and Morais Junior[51] studied HAM/TSP patients and described anterior uveitis in 11.8%, retinal vasculitis in 11.8% and vitreous opacity in 5.9%, suggesting a need to consider this etiology in endemic areas.

**Dermatological manifestations**

HTLV-associated infective dermatitis is a chronic, recurrent, eczema that predominantly affects children and adolescents. It is characterized by erythematous, scaly and crusty lesions affecting the scalp and the retroauricular, cervical, perioral, nasal and inguinocrural areas. Mild to moderate itching, chronic nasal secretions and nasal crusting are often present and patients are generally infected by *Staphylococcus aureus* and/or *Streptococcus beta haemolyticus.* Dermatitis is accompanied by an exaggerated Th1 response and elevated proviral load. Patients with HTLV and infective dermatitis are at a high risk of developing HAM/TSP (30%) and ATL.[52,53,54] Serological tests for HTLV-1 should be requested when children and adolescents present with severe and resistant forms of eczema. Differential diagnosis should aim to rule out other forms of eczema, such as atopic and seborrheic dermatitis. Infective dermatitis wounds are more exuberant, exsudative and foul smelling. Another important finding for differential diagnosis is a good response to antimicrobial treatment with sulfamethoxazole-trimethoprim.[55] Other dermatological conditions that have exhibited heightened prevalence rates in studies of asymptomatic HTLV carriers are dermatophytosis, seborrheic dermatitis and acquired ichthyosis.[56,57] Disseminated and recurrent forms of scabies have also been described in association with HTLV infections.[64]

**Arthritis and synovitis**

Cases have been described of connective tissue disease patients with HTLV-1 infections. HTLV-associated arthritis has similar clinical characteristics to idiopathic rheumatoid arthritis.

Yakova et al.[58] have demonstrated that patients with rheumatoid arthritis and other connective tissue diseases have greater proviral loads than asymptomatic carriers, in common with HAM/TSP patients. The proviral load is elevated in synovial fluid from patients with arthritis and diseases of the connective tissues.

**Infectious and parasitic diseases**

Some studies suggest that HTLV infection may be associated with immunosuppression and so increase the risk of other infectious comorbidities. *Strongyloides stercoralis* hyperinfection of patients infected with HTLV is the result of immunoresponse abnormalities that make systemic dissemination of the infestation possible, leading to recurrent chronic infection and with poor clinical response to the usual treatments.[59,60] Porto et al.[61] highlighted a possible protective effect from strongyloides against HAM/TSP, caused by a modulated Th1 response. Patients with tuberculosis have a higher rate of HTLV-1 infection than the general population.[62,63] Scabies crustosa, also known as Norwegian scabies, is a rare form of presentation that is characterized by severity and dissemination. When diagnosed it should arouse a high degree of suspicion of an HTLV coinfection, particularly if there are no other identifiable reasons for immunosuppression and in endemic areas. Scabies crustosa is correlated with poor prognosis and increased mortality.[64,65]

## Conclusions

It has been a little more than 20 years since the relationship between the HTLV virus and countless systemic diseases has been known. New perspectives have opened up on the pathophysiology of neoplastic, autoimmune and infectious diseases and even on some conditions hitherto considered degenerative. HTLV-associated diseases differ in their clinical presentation, clinical course and response to treatment, when compared to the forms observed in seronegative patients. It is important that professionals in the many different medical specialities affected become aware of these discoveries so that they incorporate this diagnostic suspicion into their daily clinical practice.

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