

## CASE REPORT

### ADULT T-CELL LEUKEMIA/LYMPHOMA ASSOCIATED WITH HTLV-1 INFECTION IN A BRAZILIAN ADOLESCENT

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#### SUMMARY

We present the case of a 15-year-old patient infected with HTLV-1 who developed a cutaneous T-cell lymphoma, confirmed by histopathological and immunohistochemical examination, as well as clinically and hematologically confirmed leukemia. The patient died 3 months after initial presentation of the disease. The rarity of the disease in this age group justifies the present report.

**KEYWORDS:** HTLV-1; Leukemia; T-cell lymphoma; Adult T-cell leukemia/lymphoma

#### INTRODUCTION

Human T-cell lymphotropic (HTLV) viruses are retroviruses classified in 2 groups, HTLV-1 and HTLV-2, which predominantly infect CD4 and CD8 cells, respectively.

HTLV-1 mainly infects inhabitants of southern Japan<sup>16,41</sup>, equatorial Africa<sup>8</sup>, Malasia<sup>50</sup>, the Caribbean<sup>6</sup>, South America (Brazil<sup>34</sup>, Colombia<sup>51</sup>, Peru<sup>19</sup>, Chile<sup>44</sup>, Argentina<sup>14</sup>, and Uruguay<sup>28</sup>), and the southern United States<sup>5,46</sup>. In Brazil, since the introduction of HTLV-1 screening tests in blood centers, the virus has been found among blood donors with a prevalence varying from state to state. The highest rate is in Bahia (1.8%) and the lowest in Santa Catarina (0.08%)<sup>2</sup>.

HTLV-1 is transmitted by the following routes: sexual<sup>21,29</sup>; parenteral, by way of blood product transfusion<sup>17</sup>; contaminated needles and syringes<sup>35</sup> and vertically, through maternal milk<sup>27,29</sup>.

HTLV-1 has been associated thus far with adult T-cell leukemia/lymphoma (ATLL)<sup>32</sup> and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP)<sup>12</sup>. The possible association of HAM/TSP with ATLL was reported by KAWANO *et al.*<sup>20</sup> and SHARATA *et al.*<sup>40</sup>, but simultaneous presentation of the two diseases in the same individual is rare. Other diseases may be associated with HTLV-1, including arthropathies, pneumopathies, uveitis<sup>11,30</sup>, and dermatologic diseases, including xerosis, eczematoid seborrhea<sup>15</sup>, crusty scabies<sup>37</sup>, balding folliculitis decalvans<sup>1</sup>, infective dermatitis<sup>24</sup>, and prurigo<sup>39</sup>. However, most HTLV-1-infected individuals do not develop any disease, thus constituting asymptomatic carriers.

The first reference to ATLL was by UCHIYAMA *et al.* in 1977<sup>43</sup> and POIESZ *et al.*<sup>32</sup>. HINUMA *et al.*<sup>16</sup> later observed the association between ATLL and HTLV-1. Subsequent studies have confirmed this association<sup>34,49</sup>. ATLL is more common in areas where HTLV-1 is endemic. Patients with ATLL are usually infected before the age of 20 years, and their relatives have a high prevalence of HTLV-1 infection. The disease does not usually appear in more than one member of the family<sup>14</sup>. Epidemiological studies focusing on ATLL demonstrate that some 2 to 4% of infected patients develop neoplasias after a latent period of 20 to 30 years, thus making it an adult disease. Sexual contact and breastfeeding are the main infection routes in these patients<sup>14</sup>. The cutaneous manifestations of ATLL are common and have different types of lesions<sup>7,10</sup>.

We present the case of a 15 year-old HTLV-1-infected patient who developed a cutaneous lymphoma of T-cell origin, confirmed by histopathological and immunohistochemical examination, and clinically and hematologically verified leukemia.

#### CASE REPORT

T.C.S., male, 15 year-old, student, mixed-race, born in Rio de Janeiro, with HTLV-1 infection diagnosed in July 1997. The patient's parents were known to be infected since 1997, and the patient denied prior sexual contact and drug use. The patient came to the Evandro Chagas Hospital/FIOCRUZ because of a erythematous infiltrating lesion on his face (Fig. 1) and papulotuberosus pruriginous cutaneous lesions on the upper limbs and torso (Fig. 2) which had appeared one month previously. Two skin biopsies were performed. Histopathological examination showed dermal infiltration of medium-to-large-sized lymphocytes with hyperchromatic

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nuclei that varied in size and shape with moderately pleomorphic lymphoid cells (Fig. 3a). These cells were more intensely and diffusely distributed in material from the ear (Fig. 3b) and mainly located around vessels in material from the upper limb. Discrete epidermotropism was present in addition to nuclear dust and rare mitotic figures (< 1/10 high power field), particularly in the sample in which the cellular infiltrate was more exuberant. Neither multinuclear tumor cells nor Pautrier microabscesses were observed. Using the immunohistochemical technique, at least half of the cellular infiltrate presented the CD45-RO antigen (Fig. 4). In the setting of positive HTLV-1 serology and a clinical picture involving skin lesions, the histopathological findings were considered compatible with ATLL. The patient soon developed adynamia and fever. The cutaneous lesions became infiltrated, and hard loose cervical lymph nodes appeared, in addition to hepatosplenomegaly. Blood cell count showed a hematocrit of 45.1% with a white cell count of 57,800, platelet count of 152,000, and lymphoid lineage with a convoluted or clover-like nuclear contour (polymorphism). Given these findings, the diagnosis of HTLV-1 associated with ATLL was made. Rapid disease progression was observed with a worsening of the skin lesions, bent and salient sternum, splenomegaly, and enlargement of the superior mediastinum. Further tests revealed LDH of 1035 U/l and

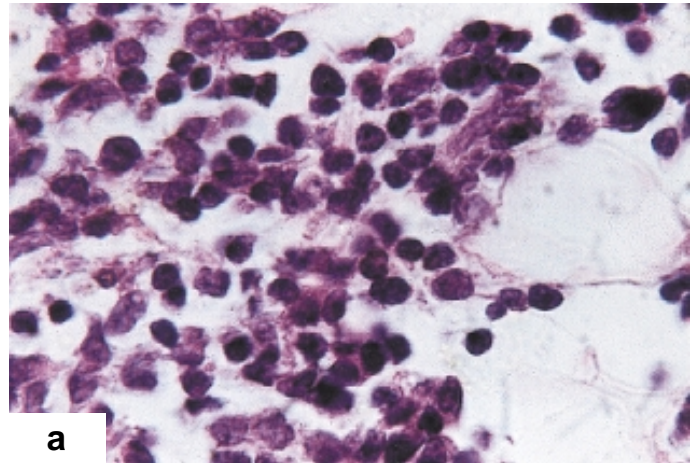
calcium of 10.7 mg/l. The patient was classified as acute-type ATLL and began treatment with alpha-interferon associated with zidovudine. No clinical response was observed, and peripheral lymphocyte levels increased. Systemic chemotherapy was begun. There was an



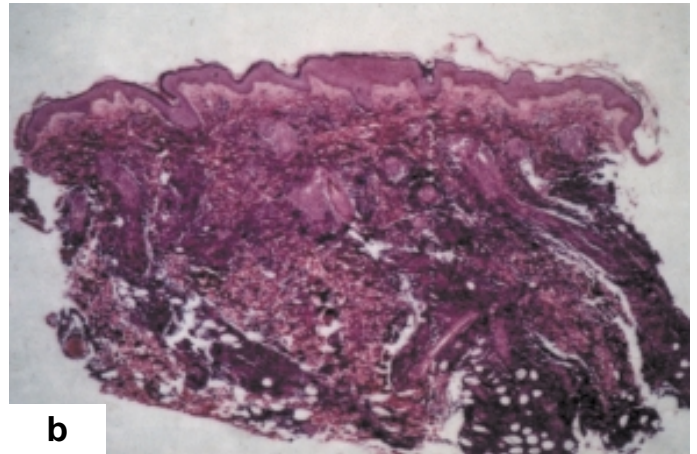
**Fig. 1** - Erythematous infiltrating lesions on the face.



**Fig. 2** - Papulotuberculous cutaneous lesions in the upper limbs and torso.

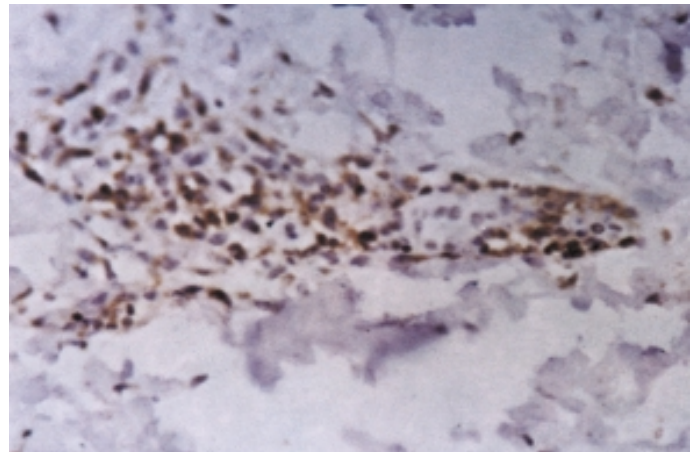


**a**



**b**

**Fig. 3** - a) Cytological detail of dermal atypical lymphoid cells. (Hematoxylin-eosin, obj x100). b) Diffuse dermal infiltrate of lymphoid cells (Hematoxylin-eosin obj X 4).



**Fig. 4** - CD45 RO+ detail lymphoid cells (immunoperoxidase technique, obj x 20).

approximately 30% reduction in the size and number of the skin lesions, although the leukemia persisted. The patient developed abdominal pain and sepsis and died after 73 days, probably due to pulmonary hemorrhage.

## DISCUSSION

HTLV-1 is endemic in some areas of Brazil, but prevalence of ATLL is still unknown. HTLV-1 infection was demonstrated in 11 patients out of a series of 14 with ATLL, using serological and/or DNA methods<sup>34</sup>. Another study in Brazil had also detected HTLV-1 infection in 26% of 188 patients with T-cell lymphoma<sup>33</sup>. The age bracket for onset of lymphoma is 40-60 years, although in a review of 28 cases of ATLL in the state of Bahia, 6 cases were found under 30 years of age<sup>3</sup>.

Our patient had no history of blood transfusion, drug use, or sexual contact, and was probably infected by breastfeeding, with a latent period of 15 years. Development of this neoplasia appears to be associated with this transmission route<sup>42</sup>. A literature review shows that ATLL is quite rare in patients under 16 years of age<sup>3,9,13,22,26,34,45,48</sup>. The term "adult T cell leukemia/lymphoma" may be inappropriate insofar as it does not occur only in adults.

In relation to the patient's family, the mother was an HTLV-1 carrier and the father, despite being the case index for HTLV-1 infection through blood donation, refused to be investigated for the disease. The patient's sister had negative HTLV-1 serology. It has been reported that individuals receiving blood transfusions with HTLV-1 develop paraparesis rather than ATLL. In a recent cohort study that included this patient, no HTLV-1 *tax* polymorphism was associated with specific manifestations of the infection<sup>36</sup>.

Concerning the patient's ethnic group, higher prevalence has been observed among black or mixed-race individuals<sup>34</sup>.

Our patient presented papulotuberculous pruriginous cutaneous lesions in the upper limbs and torso and erythematous infiltrated lesions in the face, the differential diagnosis of which included lepromatous leprosy, secondary syphilis, drug-induced eruption, and T-cell cutaneous lymphoma. The diagnosis of acute subtype ATLL was made later with the aggravation of the skin lesions and the onset of systemic leukemia symptoms detected by the blood count, hypercalcemia, increased blood LDH, and the aggressive course of the disease.

The patient initially responded well to chemotherapy, although presenting pancreatitis as a complication. He did not respond favorably to the association of alpha-interferon and AZT, contrary to the results reported by BAZARBACHI & HERMINE<sup>4</sup>, in which that regimen was beneficial in 8 of 10 patients. Three months later he developed a sudden neurological complication and he died of probable pulmonary hemorrhage.

Histologically, skin involvement in ATLL is characterized by the presence of atypical lymphocytes in focal clusters or dispersed in the dermal tissue. Epidermotropism is seen in varying degrees<sup>18,25,31,47</sup>. In one of our samples, the neoplastic cells showed a clear perivascular distribution, but without destruction of vessel walls; it has been shown that different infiltration patterns can be present when several tissue samples are obtained from different lesions in the same patient<sup>47</sup>. Since the histological alterations can be similar to those found in fungoid mycosis<sup>25</sup>, detection of HTLV-1 by tissue polymerase chain reaction can be used to diagnose these cases<sup>23,38</sup>.

In endemic areas for HTLV-1 infection, several inflammatory skin conditions can mimic ATLL, making early diagnosis and immediate treatment extremely important in light of the infection's aggressive course. In this case we identified precisely such an association, and at an early age.

## RESUMO

### Leucemia/linfoma de células T do adulto associado a infecção pelo HTLV-1 em adolescente brasileiro

Apresentamos o caso de um adolescente de 15 anos de idade com infecção pelo HTLV-1 que desenvolveu linfoma cutâneo de células T, confirmado por exame histopatológico e imunohistoquímico, assim como leucemia, diagnosticada por exame clínico e avaliação de sangue periférico. O paciente morreu 3 meses após o início da doença. A raridade da doença nesta faixa etária justifica o relato de caso.

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