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Case Report

Adult T-Cell Leukemia/Lymphoma in the Interior of Bahia: A Case Report

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Abstract: Adult T-cell leukemia/lymphoma (ATLL) is a peripheral T-cell neoplasm caused by HTLV-1, most common in endemic regions such as Japan, the Caribbean, and Latin America. This report describes the fatal case of a male patient in the state of Bahia, Brazil. ATLL is an aggressive disease with a poor prognosis, diagnosed by HTLV-1 serology and hematologic analysis. Treatment includes combination chemotherapy and antiretrovirals, but the response is usually unsatisfactory. This case highlights the importance of early diagnosis and targeted treatments. It is essential to develop more effective treatment protocols and longitudinal studies to better understand and manage the disease.

Keywords: Adult T-Cell Leukemia-Lymphoma; Human T Lymphotropic Virus Type 1; Peripheral T-cell lymphoma.

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1. Introduction

Adult T-cell leukemia/lymphoma (ATLL) is a distinct neoplasm of peripheral T lymphocytes caused by human T-cell lymphotropic virus type 1 (HTLV-1) [1], a human retrovirus that can infect CD4-positive T cells [2]. ATLL was first recognized globally in 1977 in Japan [3] and is more common in regions such as the Caribbean, and Latin America due to the endemic pattern of HTLV [4, 5].

Globally, the number of people infected with HTLV-1 may be around 20 million in some series [1, 6]. Despite the larger number of people infected with HTLV, there are no data about the financial impact of the virus in public heathy in Brazil or around the world. In addition to ATLL, HTLV-1 is associated with autoimmune and inflammatory conditions [7], such as HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) [8, 9] and HTLV-1-associated infectious dermatitis [10], in approximately half of cases [7]. Skin lesions may be the first manifestation of ATLL [7], and differential diagnoses include cutaneous T-cell lymphomas, such as mycosis fungoides [11].

In Brazil, the city of Salvador, capital of Bahia, is the epicenter of the infection [12]. In this study, we report a fatal clinical case that occurred in the interior of the state of Bahia, with the aim of providing information that contributes to the early diagnosis and treatment of the disease.

2. Case Report

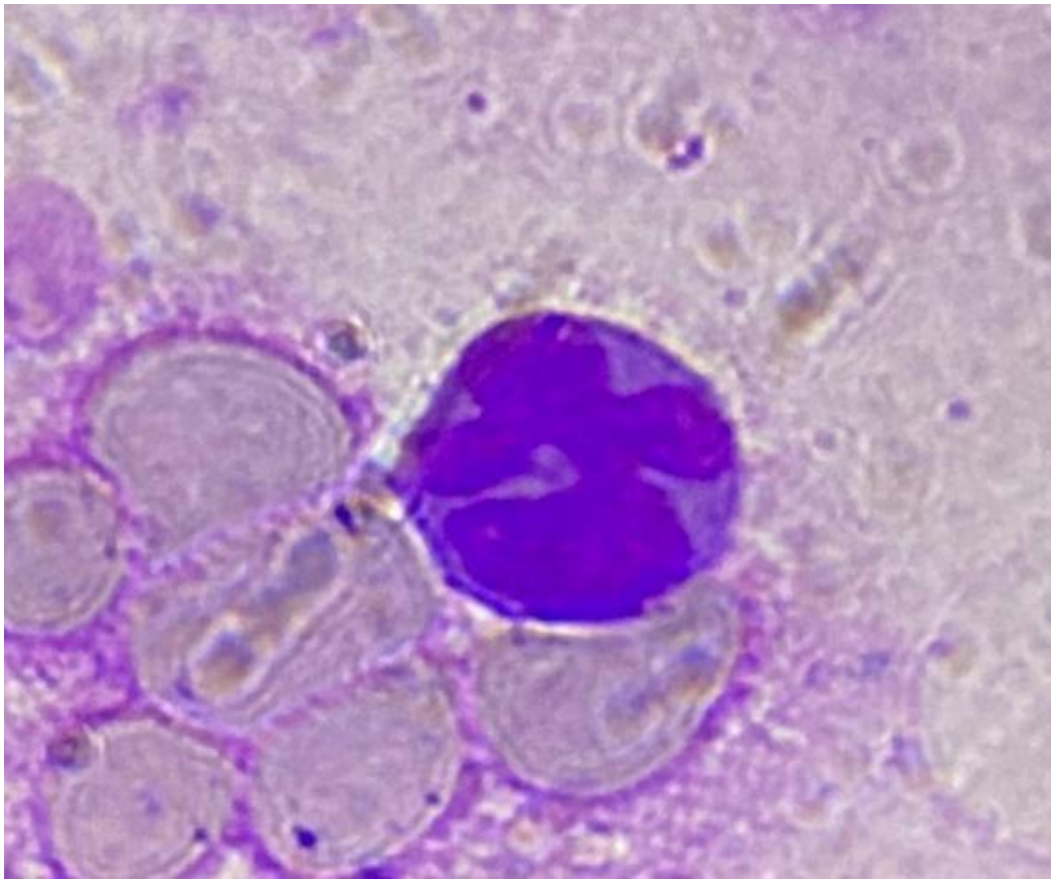
Patient, male, was admitted to the service in October 2023 referred from an external orthopedics service, with a loss of seven-kilogram one month before admission, associated with a significant increase in tumor size in the cervical and inguinal region seven days

after admission, in addition to pain refractory to tramadol and pregabalin. The physical examination upon admission presented pain and tumor size in the cervical and inguinal region. Hospitalization was chosen for investigation. Tomography of the neck, chest, and abdomen: multiple supra and infradiaphragmatic lymphadenomegaly, sometimes coalescent, forming lymph node conglomerates and central areas of necrosis, suspicious for lymphoproliferative disease.

Some lytic bone lesions in the axial skeleton are suspected of secondary neoplastic involvement. A biopsy of inguinal lymph nodes was performed late in the same month, which showed positive immunohistochemistry for CD45, lca (clone 2b11 + pd7/26), CD3, CD5 (clone 4c7), MUM 1, ki-67, CD2, CD4, and CD25. Compatible with a diagnosis of peripheral T-cell lymphoma. He continued to be monitored with outpatient chemotherapy, undergoing cytoreduction with COP and CHOEP protocol. He subsequently returned to the service brought by SAMU in January 2024 with a report of disorientation and drowsiness for three days. On examination, he was pale, confused and disoriented and with multiple cervical and submandibular lymphadenomegalies.

During hospitalization, given the refractoriness of the condition, an immunohistochemical examination of the lymph node was rescued. From then on, under suspicion of ATLL, HTLV serology was requested, confirming the diagnosis. In addition, peripheral blood microscopy revealed the presence of "flower cells" (Figure 1). It was then decided to maintain current chemotherapy and associate zidovudine.

Figure 1. Flower cell in peripheral blood smear, also known as "clover leaf cells" – Correspond to lymphocytes with condensed chromatin and bizarre hyperlobated nuclei, typical of carriers of the HTLV-1 virus [13].



The patient remained hospitalized for approximately one more month with unfavorable clinical evolution associated with complications such as endocarditis and hypercalcemia of the refractory malignancy, when proportional care was instituted. The patient passed away in April 2024.

3. Discussion

The pathogenesis of ATLL is not entirely clear, but it is believed that carcinogenesis occurs in stages, with HTLV-1 infection being the first [14], with subsequent production of oncoproteins by memory T cells [8], such as Tax and HBZ, after genomic integration [15]. The Tax protein is associated with immune evasion and proliferation, and the HBZ factor plays a similar role and aids in the transformation of T cells [15].

ATLL is frequently misdiagnosed as other mature T-cell malignancies [4,16], which is why serology, in addition to histopathological, is necessary for diagnosis, as was the case we report. Examples of differential diagnoses include mycosis fungoides and/or Sézary syndrome, cerebriform variants of T-cell prolymphocytic leukemia, peripheral T-cell lymphoma, unspecified (PTCL-U), angioimmunoblastic T-cell lymphoma, and therefore the presence of HTLV in the cells is essential to differentiate the disorders [11].

The Shimoyama classification [17] is used to classify ATLL, dividing the disease into 4 subtypes: acute, lymphoma, latent, and chronic [17]. The parameters analyzed are lymphocytosis, elevated lactate dehydrogenase, hypercalcemia, lymphadenopathy, and systemic involvement [1]. The acute form is characterized by leukemic manifestations, lymphadenopathy, organomegaly, and hypercalcemia, while the lymphoma-type form presents lymphadenopathy with or without extranodal lesions, but without lymphocytosis [17]. The latent form has a normal leukocyte count and infiltration only in the skin and lungs, and the chronic form is associated with elevated leukocyte count, lymphadenopathy, and organomegaly, without elevated lactate dehydrogenase levels or visceral involvement [17].

The prognosis, in general, is dismal, ranging from 6 months for the acute subtype to 24 months for the chronic subtype [1] and the acute and lymphoma forms have a worse prognosis despite advances in chemotherapy and transplantation [18]. Predictors of poor prognosis are elevated LDH levels, more than 4 areas involved, thrombocytopenia, bone marrow involvement, eosinophilia, hypercalcemia, being over 40 years old, p53 mutation, p16 deletions, elevated serum levels of IL-15, and expression of CC chemokine receptor 4 (CCR4) [1]. The patient in the present study presented the lymphoma form of ATLL, an aggressive presentation with a mean survival of less than 1 year.

In the morphology of peripheral blood lymphocytes, the presence of "flower cells" is suggestive of ATLL [19]. These cells are medium to large, atypical lymphocytes with multilobed nuclei with dense chromatin and small/absent nucleoli and carry the antigens tested by flow cytometry [19,20]. On flow cytometry, most ATLLs present a mature CD4 T cell phenotype [13]. Some markers are useful in the evaluation, such as CD2, CD3, CD4, CD5, CD7, CD8, CD25, CD26, CD45RO and $\alpha\beta$ T cell receptors [13], and in many there is no expression of CD7 and CD26 or decreased expression of CD3 [13].

The patient in this case presented "flower cell" in peripheral blood smear and positive immunohistochemistry for CD45, CD3, CD5, MUM 1, ki-67, CD2, CD4 and CD25, findings consistent with ATLL, at which time measures such as Zidovudine were instituted, associated with the CHOEP protocol that was already in use. Regarding the literature, the CHOP regimen or aggressive combined chemotherapy, VCAP-AMP-VECP have been the most common choices for patients with chronic, lymphoma and acute subtypes [1], with a possible association with the antiretroviral Zidovudine and IFN-α [21]. In general, cytotoxic combined chemotherapy has been the basis of therapy for aggressive type 1 ATLL.

The regimen that appears to result in the longest survival is VCAP-AMP-VECP [22], but some chemotherapy drugs used in the regimen are not sold in Brazil, making their use unfeasible in our country [23]. Because of this, the most widespread current regimen

in Brazil for ATLL is CHOP or CHOEP [23,24]. However, even with intensive chemotherapy, the outcome of aggressive ATLL remains poor [1]. Regarding hematopoietic cell marrow transplantation, autologous transplantation does not appear to be effective, but allogeneic transplantation may result in long-term disease control [13].

4. Conclusion

ATLL is a potentially fatal neoplasm, and rare and underreported lymphoma, must be suspected especially in endemic area, as Bahia state. For the diagnosis to be confirmed, serology for HTLV-1 is necessary together with the hematological and hematopathological diagnosis of peripheral T-cell leukemia/lymphoma, since morphology or immunohistochemistry alone can lead to misdiagnosis and delay treatment directed at the condition. Therefore, it is necessary to improve the tracking and combating of HTLV-1 transmission, especially in endemic regions, to make early diagnosis and treatment of ATLL possible. The treatment lacks universally applied protocols, but with CHOP or VCAP-AMP-VECP regimens being the most used, associated with Zidovudine and/or IFN-α, but with poor results even with aggressive treatments, which is why longitudinal studies on it are necessary.

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Research Ethics Committee Approval: We declare that the patient approved the study by signing the informed consent form, and that the study followed the ethical guidelines established by the Declaration of Helsinki.

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Conflicts of Interest: The authors declare no conflicts of interest.

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