T-cell prolymphocytic leukemia with cutaneous presentation: a case report

Leucemia prolinfocítica de células T com apresentação cutânea: relato de caso

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ABSTRACT

Introduction: T-cell prolymphocytic leukemia (T-PLL) is a rare hematological neoplasm that is usually aggressive and is characterized by lymph node enlargement, splenomegaly, and leukocytosis. **Case report:** this report presented a rare case of T-PLL with a cutaneous presentation similar in appearance to an allergic reaction, which challenged early diagnosis. Following diagnosis, significant treatment challenges emerged, particularly within the Unified Health System, owing to the unavailability of optimal pharmacotherapies. This resulted in an unfavourable outcome for the condition. **Conclusion:** this case revealed the difficulties in managing a rare disease within the Brazilian health system and the importance of the differential diagnosis of skin lesions with hematological neoplasms to avoid delays in diagnosis.

Keywords: Prolymphocytic Leukemia; Case Reports; Skin Diseases.

RESUMO

Introdução: a leucemia prolinfocítica de células T é uma neoplasia hematológica rara que costuma ser agressiva e apresenta-se com linfonodomegalias, esplenomegalia e leucocitose. **Relato do caso:** esse relato apresentou um caso raro de leucemia prolinfocítica de células T, com apresentação cutânea de aspecto semelhante à reação alérgica, o que dificultou o seu diagnóstico precoce. Após o diagnóstico, se evidenciou a dificuldade do tratamento, principalmente no âmbito do sistema único de saúde com a indisponibilidade das medicações ideais, acarretando em desfecho desfavorável desta condição. **Conclusão:** este caso revelou as dificuldades no manejo de uma doença rara no âmbito do sistema único de saúde brasileiro e a importância do diagnóstico diferencial das lesões cutâneas com as neoplasias hematológicas para evitar atraso no diagnóstico.

Palavras-chave: Leucemia Prolinfocítica; Relatos de Casos; Dermatopatias.

INTRODUCTION

T-cell prolymphocytic leukemia (T-PLL) is characterized by small prolymphocyte proliferation to a medium size, with a cell maturation phenotype post-thymic T involving the peripheral blood (PB), bone marrow (BM), lymph nodes, liver, spleen, and skin[1]. The first report of T-PLL was described by Catovsky (1973)[2], who attested a case of lymphoproliferative disease with cells having a lower proportion of immunoglobulins and C3 receptors on the surface with a high proportion of rosette formation with sheep erythrocytes, reported at the time as a variant of chronic lymphocytic leukemia (CLL).

Vardell (2024)[3] has indicated that T-PLL may exhibit an indolent phase in up to one-third of cases, which is a confounding factor for CLL, but with most of those cases progressing to an aggressive condition within an average of 33 months. T-PLL is a rare disease, representing 2% of lymphocytic leukemia cases in adults, mainly between 30 and 94 years (average age 65 years), seldom under 30 years[1,4]. However, it represents more than one third of mature T-cell malignancies with leukemic presentation[5].

Most patients have hepatosplenomegaly, generalized lymphadenomegaly, leukocytes greater than 100,000/mm³, and skin repercussion in more than 20% of cases. Serous effusion may occur in a minority[4]. The presence of anemia and thrombocytopenia is common mainly in the progressive form after an indolent phase of the disease and uncommon in this indolent phase[3]. Serum immunoglobulins are normal, serology for Human T-Lymphotropic Virus (HTLV) 1 and 2, and Human Immunodeficiency Virus (HIV) 1 and 2 are negative[1,3].

BM and PB showed a predominance of small to medium-sized lymphoid cells with non-granular basophilic cytoplasm with a nucleus that may be rounded, oval, or irregular with visible nucleoli[1]. In 25% of cases, the cells may be small, and the nucleolus is not visible under light microscopy (small-cell variant) and in 5% of cases, the nucleus may be aberrant and takes on a cerebriform form (cerebriform variant)[1,4]. However, bleb projections are common regardless of the shape of the nucleus[1].

Diffuse or localized maculopapular erythema is the most common cutaneous involvement and may manifest as nodular lesions or erythroderma. Skin biopsy usually shows an infiltration of lymphoid cells like those of PB in subepidermal and dermal region and may extend into the hypodermis, usually focusing on perianexial and perivascular areas[6].

T-prolymphocytes are non-terminal deoxynucleotidyl transferase (TdT) and non-cluster of differentiation 1 (CD1), and show the presence of CD2, CD3, CD5, and CD7 markers[4]. CD3 expression may be poor and usually CD52 is highly expressed and may be used as a therapeutic target[1,5]. CD4 presence and non-expression of CD8 occurs in 60% of cases, with CD4 and CD8 positive expression in 25% of cases (a very uncommon finding in other post-thymic T lymphocyte neoplasms), in addition the oncoprotein TCL1A could be overexpressed[1].

T-LPL is an aggressive disease with a one to two years survival, with some reports describing chronic cases that progressed to an aggressive form after two to three years of disease, and the best responses to treat this disease were observed with target therapy such as alemtuzumab[1,5,7].

Alemtuzumab resulted in a significant increase in survival compared to other treatments for T-PLL[5,7], this medication is an immunotherapy. It is an monoclonal antibody that binds to the CD52 antigen, predominantly expressed on T and B lymphocytes, inducing antibody and complement-mediated apoptosis[8]. However, it is typically a transient response, and it is necessary to evaluate the possible consolidation of hematopoietic stem cell transplantation (HSCT) in patients who achieve complete remission and when they are eligible[5,7].

The following is a report of a rare case of T-PLL, a rare form of leukemia, that is not included in the therapeutic protocols and guidelines of the Brazilian Ministry of Health[9]. The amount of money made available by the Brazilian Unified Health System (UHS) for the treatment of this pathology is insufficient to cover the costs of the treatment recommended as the first option, according to current literature, making the management of this case challenging in the context of the UHS[4-5,7,10]. That was approved by the ethics committee of the Hospital Geral Dr Cesar Cals under notion number 3.446.298 and CAAE 15125519.2.0000.5041.

CASE REPORT

FRS, male, 53 years old, latino, married, completed elementary school, bricklayer, presented ten months before admission with pruritic erythematous plaques in the abdomen, which progressed to cicatricial lesions in the hyperchromic macula. After four months, the

plaques progressed to the lower limbs, upper limbs, dorsal region, and face. He also reported asthenia and a reduced appetite during this period.

Seven months after the onset of symptoms, a fainting sensation triggered by effort, worsening asthenia, and a loss of seven kilograms in the usual weight were noted. Daily fever, sweating, and episodes of tremors, mainly at night started six months after the onset of the skin condition. With the worsening of the symptoms, he sought medical attention, identifying persistent lymphocytosis and abnormal cells in blood tests. Due to his complex clinical condition, he was transferred to a referral hospital.

On previous pathological history, he reported contact with cement and masonry, denied contact with paint, although working in a textile factory. He stated that he had no history of work in agriculture, smoking, alcoholism, or previous hospitalization. Approximately 16 years ago, he reported the removal of a painful lump on his left shoulder. He also related that a biopsy was conducted after the removal of a new left forearm nodule, with a benign result. In his family history, he remembered his aunt, who died due to cancer at an unknown primary site. No hematological diseases were identified in the family history.

Physical examination revealed weight loss, fever, pallor, tachycardia, light tachypnea with various cervical lymphadenopathies, exudate pharyngeal purulent and several erythematous plaques, and macules scaly hyperchromic as the final evolution of the initial skin lesion (Figure 1). Splenomegaly was noted in the abdomen, five centimeters from the left costal margin. The laboratory examination results at admission were summarized in Table 1.

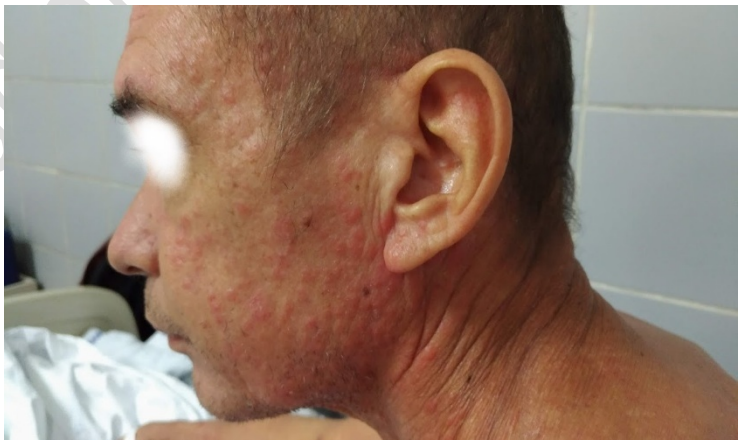

Figure 1- Erythematous plaques. Well-demarcated, raised skin lesions that are red in color. Source: the authors.

Table 1 – Admission exams. Blood count and biochemistry. Ceará, Brasil, 2025.

Exam	Result	Exam	Result
Hb	3.4 g/dl	RETIC	19,300/mm³
Ht	10%	TP	1.68
MCV	106.4 fL	aPTT	1.51
MCH	34 pg	ALB	2.8 g/dL
WBC	37,260 /mm³	GLOB	3.2g/dL
BLAST	13,041 /mm³	Ur	44 mg/dL
NEU	745/mm³	Cr	1.2 mg/dL
EO	372/mm³	Na	136 mEq/L
BAS	372/mm³	K	4.3 mEq/L
LYM	21,985/mm³	Ca	9.26 mg/dL
MONO	745/mm³	LDH	558U/L
PLAT	24,000/mm³	Uric Acid	2.6 mg/dL

The patient evaluation highlighted lymphocytosis, lymphadenomegaly, splenomegaly, and an erythematous rash formed by papule and plaques. The main hypotheses raised concerns about acute lymphoblastic leukemia, Sézary syndrome, and leukemia cutis. Flow cytometry of PB, BM aspirate, and BM biopsy was performed with T-lymphocyte proliferation at the post-thymic maturation stage (CD3 ++; CD5 ++; CD4 +; CD8-; CD20-; CD19-), with aberrant loss of CD2 E CD26 expression in 73% of the PB cells. Skin biopsy showed lymphocytic infiltrate perivascular and adnexa of cells like those in PB (CD3 +, CD5 +, CD7 +, CD4 +, CD8 +/- TdT-, and CD20). In addition, a cervical lymph node biopsy was performed and also corroborated the diagnosis by immunohistochemical analysis of a proliferation of mature T lymphocytes with CD3 expression, CD56 negativity, CD34 positivity, and TdT positivity that may also suggest a T-PLL Serological results for HIV 1 and 2 and HTLV 1 and 2 were negative.

The set of tests performed in association with the patient's clinical condition confirmed the diagnosis of T-PLL, ensuring two major criteria and one minor criterion, as shown in

Table 2, and a Fludarabine, Cyclophosphamide and Mitoxantrone (FCM) protocol was proposed once this was a treatment regimen with therapeutic potential described in the literature[7,11], and accessible within the Brazilian public health system. Human leukocyte antigen assay was collected from four siblings for referral to bone marrow transplantation.

Table 2 – Diagnostic criteria (adapted from Staber[12]). The diagnosis of T-PLL is established if all major criteria are present or if the first two major criteria and at least one minor criterion are present. Ceará, Brasil, 2025.

Major criteria	Minor criteria
>5000/mm^3 cells of T-PLL phenotype in PB or BM	Abnormalities in chromosome 5,12,13,22, or complex karyotype
T-cell clonality	Abnormalities involving chromosome 11 (11q22.3; Ataxia Telangiectasia Mutated (ATM))
Genetic abnormalities of 14q32 or Xq28 or expression of TCL1A/B, or MTCP11	Abnormalities in chromosome 8
	Involvement of T-PLL specific site

After two FCM cycles, the patient maintained the fever and skin lesions, performed a new study from the BM, which was still infiltrated by T-PLL, and it was not possible to provide therapy with alternative treatments such as alemtuzumab or clinical trials, because it was unavailable by the Unified Health System and the lack of regulation by National Health Surveillance Agency for the use of this medication for T-PLL, requiring acquisition through the supplier laboratory's social assistance program. However, the patient developed infectious complications and died six months after diagnosis.

DISCUSSION

Our case drew attention to skin lesions associated with a possible history of exposure to materials with potential allergens that initially had a difficult diagnosis of allergic reaction, however the presence of weight loss, visceromegaly, and lymphocytosis motivated referral to the referral service.

The main hypothesis was that lymphoproliferative disease mainly questioned the possibility of cutaneous disease given the exuberant skin presentation, and considered Sézary

disease and mycosis fungoides, along with the assumption of acute lymphocytic leukemia associated with leukemia cutis.

The main differential diagnoses of T-PLL are adult T-cell leukemia, T lymphoblastic leukemia, Sézary syndrome, disseminated peripheral T-cell lymphoma, and T-large granular lymphocytic leukemia[13]. The presence of more than 5,000/mm³ cells of T-PLL phenotype in PB, the proven T-cell clonality by immunophenotyping and immunochemistry of lymph node, and the involvement of the skin confirmed the diagnosis of T-PLL.

While some T-PLL patients may initially present as a stable and indolent course, with low-burden disease, our case report presented as an aggressive form with multisystemic involvement (skin involvement, lymphadenopathy, esplenomegaly, unintentional weight loss of more than 10% of normal body weight, night sweats, sporadic fever and severe anemia). Therefore, there was a clear indication of treatment with best available treatment in our institution according to consensus implemented by the T-PLL International Study Group[12]. The definitions of treatment indication were resumed in Table 3 below.

Table 3 – Treatment criteria (adapted from Staber[12]). The treatment of T-PLL is indicated if at least one of the criteria below is present. Ceará, Brasil, 2025.

Criteria	Definition
Constitutional symptoms	Significant fatigue (ECOG ≥ 2) Unintentional weight loss > 10% in ≤ 6 months Night sweats without infection Fever > 38 °C without infection
Symptomatic bone marrow failure	Hemoglobin < 10 g/dL, Platelets < 100,000/mm³
Rapid lymph node, spleen, or liver enlargement	Increase > 50% in longest diameter within 2 months or doubling in < 6 months
Progressive lymphocytosis	Lymphocyte count > 30 × 10⁹/L with > 50% rise in 2 months or doubling time < 6 months
Symptomatic extranodal involvement	Organ infiltration (e.g., skin), pleural or peritoneal effusion, central nervous system involvement

As observed by Jain et al. (2017)[14] in a historical cohort conducted at a cancer center in southern India, with 119 patients evaluated between 2010 and 2015, splenomegaly occurred in 38% of individuals, while 28% had skin lesions. The median survival was 19 months, using treatment regimens based on alentuzumab. In a case study in Latin America (Chile), a 58-year-old patient progressed rapidly to hepatosplenomegaly and skin infiltrates, without immediate access to target therapies. Five months after the onset of symptoms, the patient had a fatal outcome, having undergone two cycles of conventional chemotherapy[15].

After diagnostic confirmation, due to the unavailability of alemtuzumab as the first-line therapy, the FCM scheme was chosen, with is described as having an overall response rate (ORR) of 68% (considering complete and partial remission)[4,11]. Ideally, it should be followed by consolidation with alemtuzumab, wich presents an overall response rate of 90%[4,11]. Patients achieving complete or partial remission after therapy should be considered for an allogeneic stem cell transplant, since around one third may present long-term survival with this approach[16].

A multicentre study by the German CLL Study Group, evaluating the FMC (Fludarabine, Mitoxantrone, and Cyclophosphamide) protocol followed by alemtuzumab, achieved and median survival significantly superior to conventional regimens[11]. A multicentre European report has demonstrated that the utilisation of first-line alemtuzumab in conjunction with bone marrow transplantation has yielded an overall survival rate of approximately 48% at the six-year mark[17].

Despite the initiation of the available chemotherapy protocol in our service, the patient in this case report progressed to an unfavorable outcome due to therapeutic failure and a severe infection as adverse effect, which was the cause of death.

CONCLUSION

This case reveals the difficulty of early diagnosis of rare diseases and the need to remember that the differential diagnosis of skin lesions can be complex and should include hematological neoplasms among the diagnostic possibilities. In addition, limitations of the Brazilian Health System in terms of therapeutic options for the treatment of T-PLL is a factor that makes the ideal hematological management of this disease difficult, and, therefore, a higher chance of unfavorable outcome for these patients. However, even in ideal situations

(ie, the availability of alemtuzumab), the prognosis of T-PLL is usually poor. This case highlights the need for implementing new antineoplastic medication into our public health care system and their approval by the National Health Surveilance Agency.

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