

Cutaneous T-cell lymphomas: diagnosis and treatment challenges in Angola and Sub-Saharan Africa

Linfomas cutâneos de células T: desafios no diagnóstico e tratamento em Angola e na África Subsaariana

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Abstract

Cutaneous T-cell lymphomas (CTCLs) are a heterogeneous group of rare diseases, for which there is little epidemiological data in Angola and Sub-Saharan Africa (SSA). Diagnosing CTCLs requires a systematic evaluation of general symptoms, skin lesions, and histological features to guide their management. Mycosis fungoides (MF) is the most common non-Hodgkin's lymphoproliferative disease, followed by cutaneous anaplastic CD30+ large cell lymphoma (ALCL), accounting for about 2-5% of non-Hodgkin's lymphomas. We present the clinical, histopathological, and immunohistochemical features, therapeutic approach, and outcomes of the first two well-documented cases of anaplastic lymphoma kinase-negative ALCL CD30+ and MF in Angola, illustrating the challenges for diagnosing and managing such malignant diseases in that context. A succinct literature review highlights the characteristics of these tumors in darker skin types, i.e., skin of color patients, and reports from SSA.

Keywords: Cutaneous T-cell lymphomas. Mycosis fungoides. CD30 + anaplastic lymphoma. Biomarkers. Angola.

Resumo

Os linfomas cutâneos de células T (LCCTs) constituem um grupo heterogêneo de doenças raras, sobre as quais existem poucos dados epidemiológicos em Angola e na África Subsaariana (ASS). O diagnóstico requer uma avaliação sistemática dos sintomas gerais, lesões cutâneas e características histológicas para orientar o seu manejo. A micose fungoide (MF) é a doença linfoproliferativa não Hodgkin mais comum, seguida pelo linfoma cutâneo anaplásico de grandes células (LCAG) CD30+, que representam cerca de 2-5% dos linfomas não Hodgkin. Este relato descreve as principais características clínicas, histopatológicas e imuno-histoquímicas, abordagem terapêutica e o desfecho dos dois primeiros casos bem documentados de LCAG CD30+ ALK-negativo e de MF em Angola, ilustrando os desafios para o diagnóstico e manejo desses tumores nesse contexto. Uma breve revisão da literatura destaca as características dos LCCTs em pacientes com pele pigmentada e em relatos da África Subsaariana (ASS).

Palavras-chave: Linfomas cutâneos de células T. Micose fungoide. Linfoma anaplásico CD30+. imuno-histoquímica. Angola.

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Introduction

Cutaneous T-cell lymphomas (CTCLs) are a heterogeneous group of rare diseases, for which there is a paucity of epidemiological data in sub-Saharan Africa (SSA).¹⁻⁴ There is a lack of large-scale, prospective studies, and current data are often retrospective, incomplete, and inconclusive. Diagnosis requires a systematic evaluation of the skin lesions and systemic symptoms, as well as a careful histological examination to guide management decisions.^{4,5}

Among the various CTCL subtypes, the most common are mycosis fungoides (MF) and its leukemic presentation, Sézary Syndrome (SS) – representing 60-70% of CTCLs – followed by cutaneous anaplastic CD30+ large cell lymphoma (ALCL).^{2,5} CTCLs make up approximately 4% of all non-Hodgkin lymphomas in the US and have an overall incidence of 0.6-0.7/100,000 person-years.¹ While there are no studies that estimate the prevalence of CTCLs or MF in SSA, CTCLs have been reported to occur with a higher incidence rate and worse outcomes among African American patients.^{1,3}

The incidence of ALCL is more common in males and has a bimodal peak, occurring during adolescence and at age 60. Lymph node involvement is common. Approximately 80% of ALCL cases present with the Anaplastic Lymphoma Kinase (ALK) mutation. ALK-negative ALCL cases are more common in older adults. No causative agents or predisposing factors have so far been demonstrated, but patients with human immunodeficiency virus (HIV) have weakened immune systems that increase the risk of ALK-negative ALCL.^{1,2,4}

This is a retrospective descriptive study of a case of cutaneous ALCL and of a case of MF, admitted, respectively, at the Luanda and Huambo services of dermatology;⁶ we report the main clinical, histopathological, and immunohistochemical features, therapeutic approach, and outcomes of these two cases, highlighting the local diagnostic and management challenges.

Case report

Case 1

Case 1 was a phototype VI, a 54-year-old male with no relevant pathological history, presenting with a 6-month evolution of osteomyoarthralgias, anorexia, and general malaise, followed by marked weight loss, fever, and diffuse abdominal pain, with vomiting and diarrhea, leading to his hospital admission. Clinical findings on admission at the Dermatology Service of

the Viana General Hospital (Fig. 1A-C) showed a wasted patient with poor general and nutritional condition, multiple lymphadenopathies, and a soft and painful abdomen with hepatomegaly; both thighs presented numerous dermal, infiltrated, erythematous, sometimes ulcerated 1-3 cm large tumoral nodules, painless and adherent to the superficial and deep planes.

Additional investigations showed a normal blood count, negative HIV and venereal disease research laboratory (VDRL) testing, and a chest X-ray without visible alteration. Bone marrow biopsy was not done due to technical limitations. A chest and abdominal computed tomography scan showed expansive lesions of irregular contrast absorption, localized to the skin and subcutaneous tissue, without a defined cleavage plane; enlarged axillary lymph nodes; absence of mediastinal involvement; and hepatomegaly and lymph node enlargement on the abdominal ultrasound.

The histopathologic and histochemical examination of a tumoral nodule showed the features of a cutaneous ALCL, with a diffuse dense dermal cellular proliferation and sheets of cells arranged in a vaguely nodular pattern (Fig. 2A and B). On high magnification (Fig. 2C), eosinophilic cellular cytoplasm, markedly pleomorphic nuclei, and, sometimes, evident nucleoli; exuberant mitotic activity, without necrosis.

The immunochemistry examination showed strong and diffuse positivity for the CD30 T-marker (Fig. 3A), as well as positivity for LCA and CD3 with reduced expression in relation to CD30; negativity for ALK (Fig. 3B), as well as for AE1/AE3, Sox10, CD20, and epithelial membrane antigen markers.

Case 2

Case 2 was a phototype VI, 74-year-old male, with a prolonged history of unspecified allergy treated with unknown products, including phytotherapy; the patient was admitted to the Dermatology Service of the Huambo General Hospital in poor general condition for widespread polymorphic cutaneous lesions, depressed consciousness, edematous face and limbs, lymphadenopathies, slightly pale mucous membranes, dehydration, hypothermia, dyspnea, bradycardia (50/min), and inconspicuous arterial tension.

Figure 4 shows the multiple polymorphic, infiltrated, sometimes ulcerated skin lesions of various sizes ($\pm$ 0.5-2 cm) with necrotic and crusted centers, dirty bottoms covered by purulent secretions, on edematous, hyper/hypo pigmented, and xerotic bases. Mucous membranes showed oral erosive lesions, bilateral



Figure 1. Case 1 clinical findings **A-C**: lower limbs showing on both thighs numerous dermal, infiltrated, erythematous, sometimes ulcerated 1-3 cm large painless tumoral nodules, adherent to the superficial and deep planes.

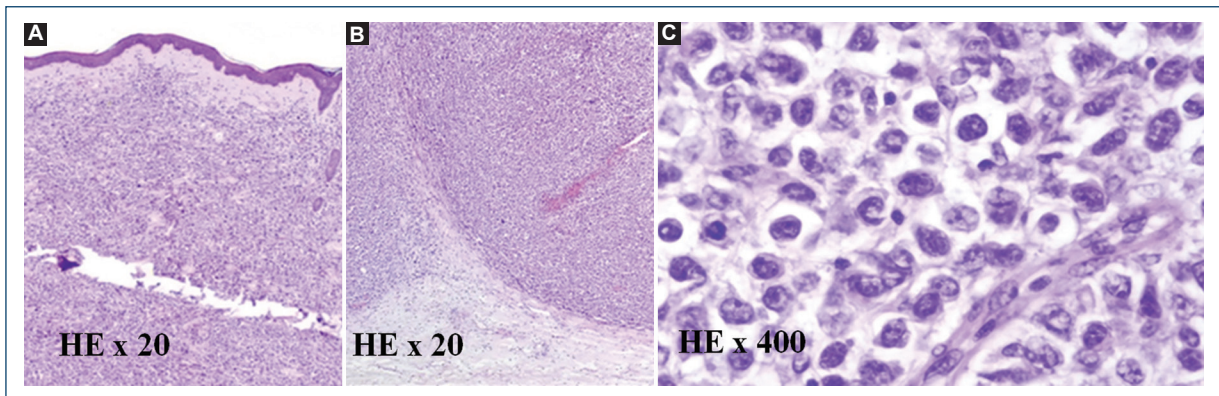


Figure 2. Case 1 histopathological findings. **A**: diffuse dense dermal cellular proliferation; **B**: sheets of cells arranged in a vaguely nodular pattern (H&E $\times$ 20); **C**: eosinophilic cellular cytoplasm, markedly pleomorphic nuclei, and, sometimes, evident nucleoli. Exuberant mitotic activity, without necrosis (H&E $\times$ 400).

orbital edema, and purulent discharge. Hair and nail alterations were characterized by diffuse alopecia, nail hyperkeratosis, onychogryphosis, and melanonychia. Genitals showed ulcerations with central necrosis. The patient passed away with sepsis and multiorgan failure 9 days after hospital admission.

Initial laboratory evaluation showed a white blood cell count of 11,550/mcL with marked eosinophilia (67.5%), mild anemia (hemoglobin 10.7 g/dL and low hematocrit 27.8%); platelets within normal range (220'000/mcL); HIV, VDRL, hepatitis C virus, and HbS negative. Bone

marrow biopsy and blood culture were not performed due to laboratory limitations.

The routine 2023 hexachlorocyclohexane histopathological report – without pictures – by the local Huambo pathologist suggested the diagnosis of MF; a repeat histopathological plus immunohistochemistry examination in 2025 of the same biopsy material, by a private laboratory in Luanda, showed a T-cell lymphocyte dermal infiltrate with some epidermotropism (Fig. 5A), together with a predominance of CD3 and CD4 T markers (Fig. 5B) and loss of CD5, CD7, and CD8. Typical

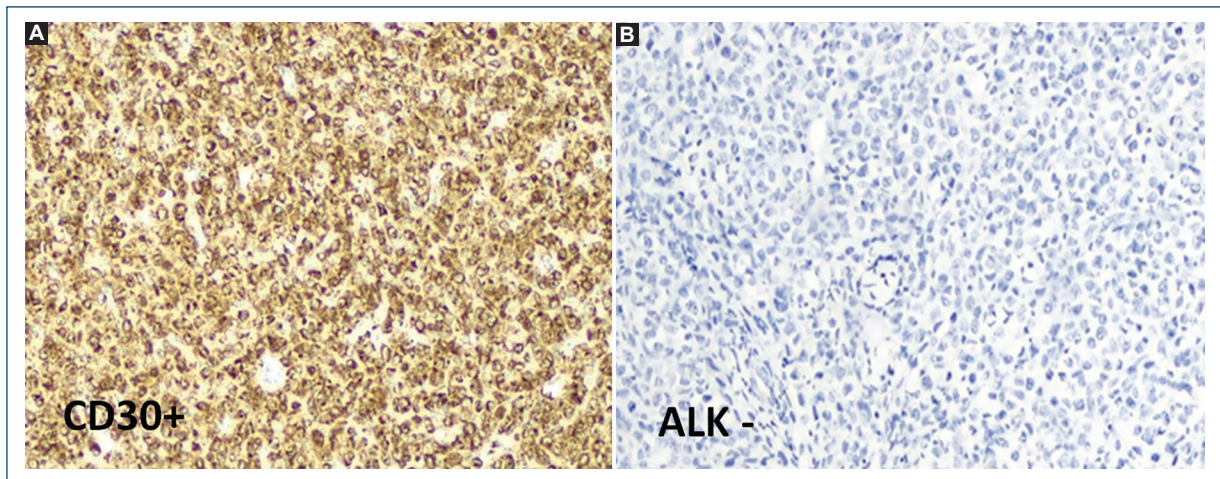


Figure 3. Case 1 immunohistochemistry findings: **A:** strong positivity for CD30 marker; **B:** negative reaction for anaplastic lymphoma kinase.



Figure 4. Case 2: multiple polymorphic, infiltrated, sometimes ulcerated skin lesions with necrotic and crusted centers, of various sizes $\pm$ 0.5-2 cm, with dirty bottoms covered by purulent secretions, on edematous, hyper/hypo pigmented and xerotic bases.

Pautrier's microabscesses were not observed. Periodic acid-Schiff staining was negative.

Discussion

Except for some suspected cases of MF and SS diagnosed on a clinical basis, there are no epidemiologic data on CTCLs in Angola. The two reported patients were the first ones confirmed by biopsy and immunohistochemistry. Early clinical recognition of CTCLs is compounded by the scarcity of trained dermatologists, difficult diagnosis on a clinical basis only, patients' presentation often at an advanced stage, and difficult follow-up on an ambulatory basis.

The highly variable cutaneous manifestations of CTCLs, including those of their multiple subtypes and variants, compound the clinical diagnosis of these lymphoproliferative disorders. In case 1, the initial clinical diagnosis spanned other mimicking conditions, including deep mycosis, Kaposi sarcoma, bacillary angiomatosis, leishmaniasis, and sarcoidosis, which were eventually excluded histopathologically.

ALCL diagnosis confirmation always requires one or more skin biopsies, with routine histopathology and immunohistochemistry, to reveal the atypical, large anaplastic cells, which show diffuse, strong positivity for the CD30 antigen. The symptoms, clinical skin lesions, histology, and histochemical features observed in our advanced ALCL case were fully consistent with those reported in the literature.³

One of the challenges in the early recognition of MF is the difficulty in differentiating the disease from benign inflammatory disorders, such as atopic dermatitis, chronic eczema, and psoriasis.⁷ The mean duration between the appearance of skin lesions and the histological diagnosis of MF is 8-10 years.⁵ Our case was admitted at an advanced age and stage, with signs of superinfection, leading to considering initially in the differential diagnosis other conditions, such as drug reaction and ecthyma gangrenosum. The diagnosis of MF is notoriously difficult and may take some time to be confirmed,^{7,8} especially in limited settings; the correlation between the history and symptoms, the multiple and variable skin lesions of case 2, together with

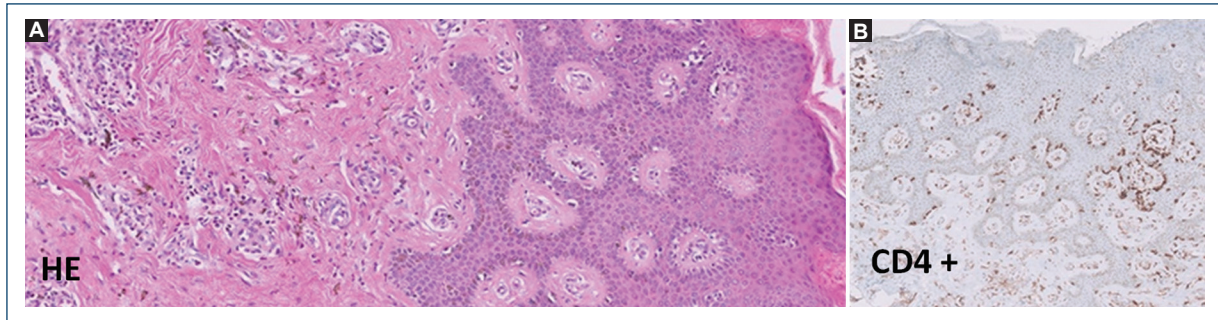


Figure 5. Case 2 histopathological and immunohistochemical findings; **A:** dermal T-cell lymphocyte infiltrate with epidermotropism (HE, low magnification); **B:** predominance of CD4 T-markers.

the initial routine histopathology, led, in 2023, to suggest the diagnosis of MF. In 2025, the reassessment of the routine histopathology, plus an immunohistochemical examination, supported the same diagnosis. Besides, it was noted that the marked eosinophilia and the increased risk of sepsis-specific death observed in our case have been reported in black patients with MF.^{1,3,5}

Angola's National Health Service histopathology facilities – particularly at subnational level – are still scarce and deficient in trained skin histopathologists and often lack a microscope camera to document difficult cases. Moreover, the frequent lack of immunohistochemical reagents necessitates seeking assistance from private or foreign laboratories to confirm the diagnosis.

Due to the very limited availability of phototherapy, radiotherapy, chemotherapeutic, and immunobiological agents, management is often symptomatic, and patients are difficult to follow up on an ambulatory basis. The first reported patient died out of hospital, without any targeted specific treatment; Case 2 passed away 9 days following hospital admission from sepsis and severe multiorgan failure.

Conclusion

The diagnosis and management of CTCLs are generally difficult in SSA due to the polymorphic clinical features, the need for multiple biopsies, deficient histopathology and immunohistochemical facilities, as well as the common lack of appropriate chemotherapy agents. Some research suggests that CTCLs, such as MF, may be more common in people of African descent; there is thus a need to improve diagnostic methods⁷ and epidemiological knowledge through prospective and collaborative studies across Africa to collect data

on specific CTCL subtypes. Despite their low incidence, greater awareness and knowledge of these malignant diseases are required in Angola, considering the higher incidence rate and poor survival outcome among darker skin type (skin of color) patients. This is a situation that needs urgent correction in order to reduce the morbidity and mortality from cutaneous lymphomas and severe skin diseases.

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Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence.

The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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