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Case Report

An ALK-Positive Anaplastic Large Cell Lymphoma with Striking Cutaneous Manifestations and Diagnostic Insights

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Abstract

Introduction: Secondary Cutaneous Lymphomas (SCL) result from nodal or extranodal lymphoma dissemination and are characterized by skin infiltration. Diagnosing SCL is complex and requires clinical, histopathological and molecular evaluations. SCL can present with diverse manifestations, with disseminated lesions indicating a poor prognosis. This report describes a rare case of ALK-positive Anaplastic Large Cell Lymphoma (ALCL) with cutaneous involvement.

Case Report: An 18-year-old male presented with an eight-month history of a tumoral lesion with serohematic crusts on the anterior thoracic region and satellite erythematous-violaceous nodules. No systemic B symptoms were reported. Histopathology revealed a diffuse proliferation of large pleomorphic lymphoid cells in the dermis and hypodermis. Immunohistochemistry showed strong positivity for CD30, EMA and ALK, supporting the diagnosis of secondary cutaneous involvement by ALK-positive nodal/systemic ALCL. Bone marrow biopsy confirmed lymphoma infiltration. The patient was referred for surgical and hematological evaluation and initiated chemotherapy protocols.

Discussion: SCL accounts for up to 50% of cutaneous lymphomas and presents as nodules, plaques or ulcerations. Disseminated lesions within six months of diagnosis reduce survival rates significantly. Accurate differentiation between primary and secondary lymphoproliferative diseases requires imaging, bone marrow biopsy and molecular techniques. Treatment includes chemotherapy, radiotherapy and emerging therapies such as checkpoint inhibitors, CAR-T cells and targeted agents like brentuximab vedotin. ALK-positive ALCL is generally associated with a more favorable prognosis compared to ALK-negative subtypes.

Conclusion: Early diagnosis and intervention are critical for improving survival in SCL patients. Dermatologists play a crucial role in recognizing these lesions and initiating multidisciplinary management.

Keywords: Secondary Cutaneous Lymphoma; ALK-Positive Anaplastic Large Cell Lymphoma; Cutaneous Dissemination; Immunohistochemistry; Multidisciplinary Management; Oncology

Abbreviations

SCL: Secondary Cutaneous Lymphomas; ALK: Anaplastic Lymphoma Kinase; ALCL: Anaplastic Large Cell Lymphoma; CD30: Cluster of Differentiation 30; EMA: Epithelial Membrane Antigen; CD45RO: Cluster of Differentiation 45RO; CD4: Cluster of Differentiation 4; CAR-T: Chimeric Antigen Receptor T-Cell Therapy; SUS: Sistema Único de Saúde; sALCL: Systemic Anaplastic Large Cell Lymphoma; ORR: Overall Response Rate; CRR: Complete Response Rate

Introduction

Secondary Cutaneous Lymphomas (SCL) are characterized by cutaneous infiltration resulting from the dissemination of nodal and extranodal lymphomas [1]. Their diagnosis is complex, as it involves multiple clinical, histopathological and molecular factors. SCL can present with a wide range of clinical manifestations; however, disseminated lesions are associated with a poorer prognosis [2]. Early detection of these extranodal lesions significantly improves the chances of better survival outcomes. This case report describes a patient diagnosed with an anaplastic large cell lymphoma that is positive for Anaplastic Lymphoma Kinase (ALK) [3].

Case Report

An 18-year-old male presented with a tumoral lesion with serohematic crusts in the anterior thoracic region, persisting for eight months with progressive growth. He also developed erythematous-violaceous satellite nodules scattered across the skin (Fig. 1). The patient denied fever, pruritus, excessive sweating or weight loss.

An incisional biopsy was performed and the histopathology revealed a diffuse proliferation of large, pleomorphic lymphoid cells with hyperchromatic nuclei in the dermis and hypodermis, displaying sparse cytoplasm and an unorganized arrangement (Fig. 2). Immunohistochemical analysis demonstrated strong diffuse positivity for CD30, EMA and ALK, along with focal expression of CD45RO and CD4 (Fig. 3). These findings supported the diagnosis of secondary cutaneous involvement by ALK-positive nodal/systemic anaplastic large cell lymphoma. This conclusion was reinforced by the fact that primary anaplastic large cell lymphomas of the skin (CD30-positive primary cutaneous T-cell lymphoproliferative disorders) rarely exhibit ALK translocations and commonly present a diffuse CD4 pattern [3].

A subsequent bone marrow biopsy revealed infiltration by anaplastic large lymphoid cells with a similar immunohistochemical profile. The patient was referred to hematology and surgical oncology for evaluation of potential surgical intervention and initiation of early chemotherapy protocols. Due to resource limitations in the Brazilian Unified Health System (SUS), cytogenetic and molecular tests, such as Fluorescence In Situ Hybridization (FISH), could not be performed to detect ALK gene rearrangements. Although these tests are essential for confirming the diagnosis of Anaplastic Large Cell Lymphoma (ALCL) and determining ALK status, lack of access to these technologies is a common challenge in many public healthcare systems.

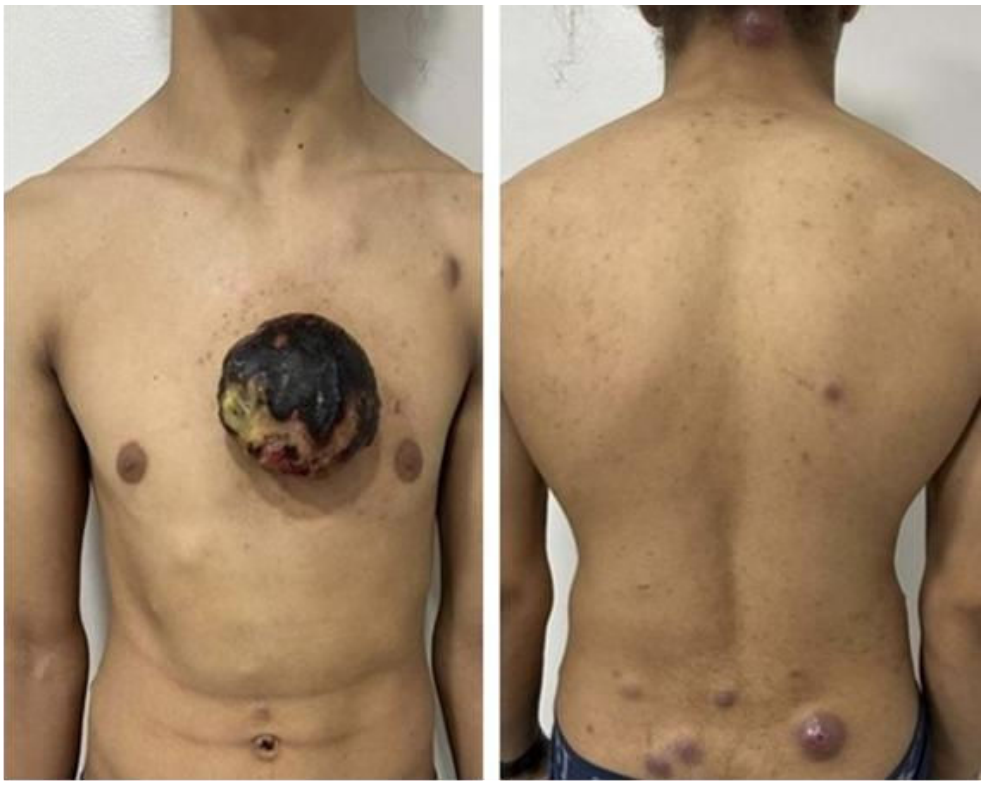

Figure 1: Exophytic tumor on the anterior thorax and isseminated erythematous-violaceous nodules across the skin.

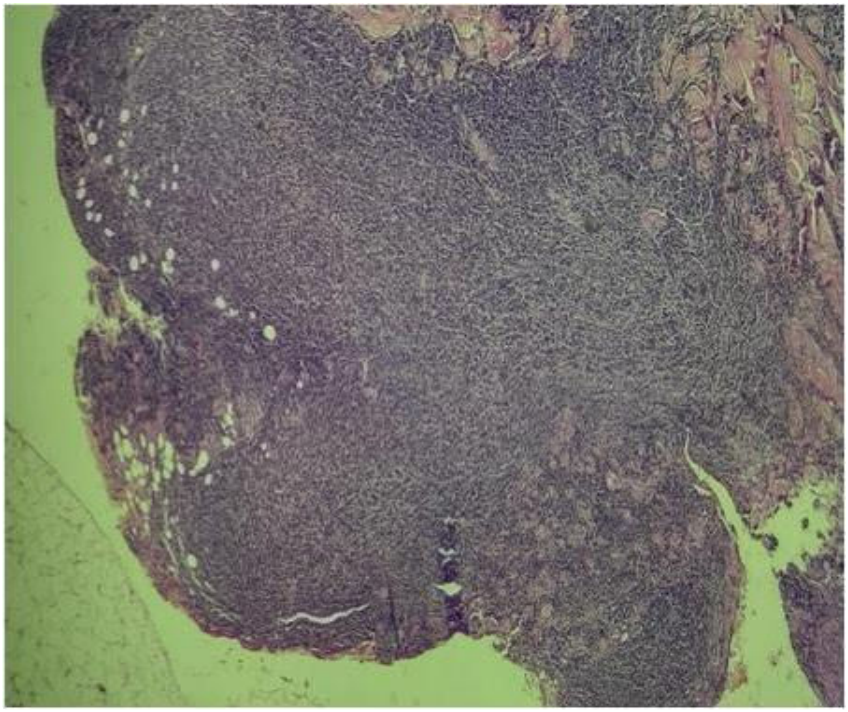

Figure 2: Lymphoid proliferation of large, discohesive anaplastic cells infiltrating the dermis and hypodermis (H&E, 4x objective).

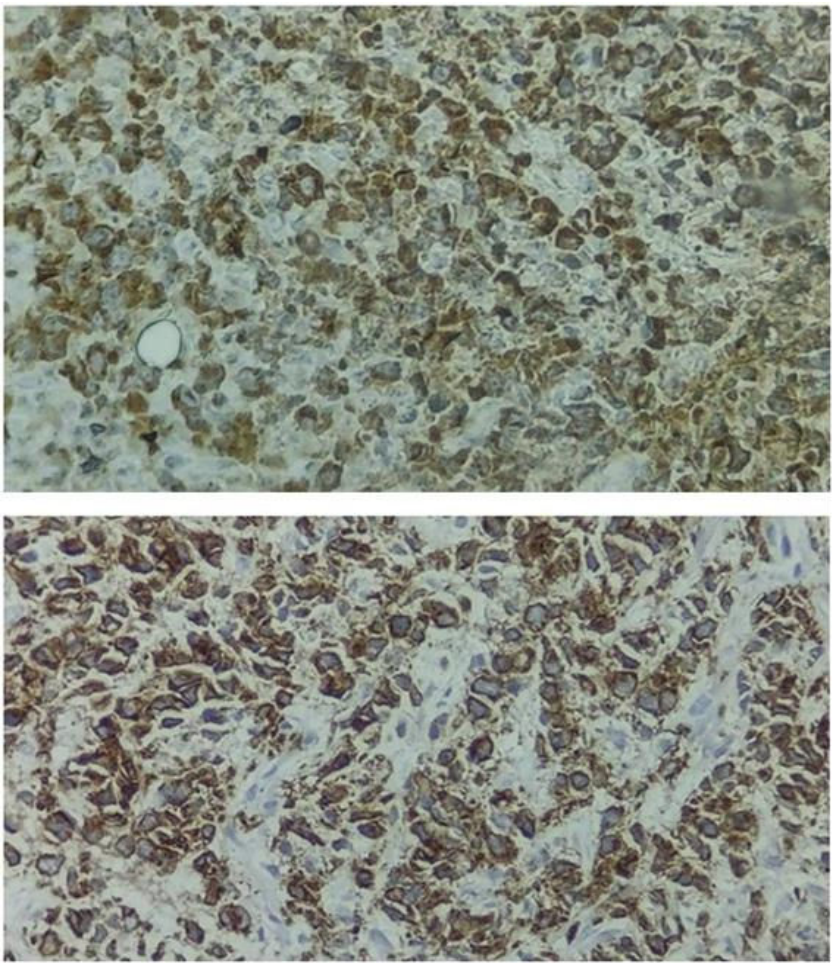

Figure 3: Immunohistochemistry (10x objective) showing strong and diffuse positivity for CD30 (top image) and ALK (bottom image).

Discussion

SCLs account for up to 50% of cutaneous lymphomas and can be classified as either T-cell or B-cell in origin [4]. Their clinical presentation is highly variable, encompassing nodules, macules, plaques, and, less frequently, ulcerations. Cutaneous dissemination within the first six months of diagnosis is associated with reduced survival rates, with approximately 31% of patients surviving beyond five years. Disseminated lesions further contribute to an unfavorable prognosis. In contrast, primary cutaneous lymphoproliferative disorders generally follow an indolent course, with survival rates ranging from 87% to 92.5% [2]. Distinguishing primary from secondary lymphoproliferative diseases solely based on clinical, histopathological and immunohistochemical criteria is often insufficient. Additional diagnostic tools such as imaging, bone marrow biopsy, blood flow cytometry and other molecular techniques are essential for accurate staging, precise subtyping and appropriate classification [5].

The treatment of SCL includes isolated radiotherapy or a combination of radiotherapy and chemotherapy in cases with extracutaneous involvement. Emerging therapeutic approaches, such as immunotherapy with checkpoint inhibitors, CAR-T cell therapy and targeted agents like brentuximab vedotin, ibrutinib, acalabrutinib and idelalisib, have shown promising outcomes [6,7]. The comparison of the efficacy of CAR-T cell therapies, checkpoint inhibitors and targeted therapies such as brentuximab vedotin in the treatment of Secondary Cutaneous Lymphoma, particularly in cases of ALK-positive ALCL, is an evolving field of study. Brentuximab vedotin, an antibody-drug conjugate that targets CD30-expressing malignant cells, has demonstrated significant efficacy in relapsed or refractory systemic ALCL. In a multicenter phase II study, the Overall Response Rate (ORR) was 86%, with a Complete Response (CR) rate of 66% [8]. Efficacy was similar in patients with ALK-positive ALCL, with an ORR of 81% and a CR rate of 69% 8. The 5-year Overall Survival (OS) rate was 56% for patients with ALK-positive ALCL [8]. Regarding CAR-T therapies, there are case reports exploring the use of CD30-targeted CAR-T cells in ALK-positive ALCL, particularly in relapsed/refractory disease scenarios. One reported case described the use of crizotinib and brentuximab vedotin as a bridge therapy for autologous stem cell transplantation, followed by CD30-targeted CAR-T cell therapy, resulting in complete remission and long-term disease-free survival [9]. However, further prospective studies are needed to confirm the efficacy of this approach. Checkpoint inhibitors, while promising in other types of lymphomas, still lack robust specific data for ALK-positive ALCL in Secondary Cutaneous Lymphoma. The combination of brentuximab vedotin with immunotherapy or other targeted agents, such as ALK inhibitors, is being investigated to improve clinical outcomes [10].

In this case, the cutaneous involvement of ALK-positive anaplastic large cell lymphoma was characterized by papules, nodules, non-tender lymphadenopathy and the absence of B symptoms (fever, night sweats and weight loss). ALK-positive ALCL is generally associated with a more favorable prognosis compared to ALK-negative ALCL. This is largely due to the presence of the NPM-ALK translocation, which is more common in younger patients and is associated with better clinical outcomes. For systemic ALCL, ALK-positive cases have 5-year survival rates ranging from 70% to 90%, whereas ALK-negative cases have lower survival rates, typically between 40% and 60% [8,11,12]. The favorable prognosis of ALK-positive ALCL is attributed to its responsiveness to standard anthracycline-based chemotherapy regimens, such as CHOP (Cyclophosphamide, Doxorubicin, Vincristine and Prednisone) [8,11]. The management of ALK-negative ALCL often involves more aggressive treatment strategies, including the potential use of consolidative autologous stem cell transplantation in certain cases [8,11]. In terms of therapeutic response, both ALK-positive and ALK-negative ALCLs are treated with anthracycline-based chemotherapy as the first-line approach. However, ALK-negative cases may require additional therapeutic interventions due to their less favorable response to standard chemotherapy [8,11]. These differences have important implications for the treatment and management of patients with secondary cutaneous lymphoma, highlighting the importance of a personalized and evidence-based approach.

It is important to highlight that this case report describes a single patient, which significantly limits the generalizability of the findings. While it provides valuable insight into the clinical and histopathological presentation of ALK-positive ALCL with cutaneous involvement, the conclusions drawn should be interpreted with caution. Larger cohort studies or multicenter analyses are needed to confirm whether these findings are applicable to broader populations and to establish stronger associations between clinical features and outcomes. Further research is warranted to explore personalized therapeutic strategies for ALCL with cutaneous involvement, particularly those guided by biomarker-driven approaches. Additionally, population-based studies are necessary to assess the epidemiology, genetic variations and treatment responses in diverse patient cohorts, which may reveal prognostic factors and novel therapeutic targets. Expanding our understanding of ALCL subtypes and their response to emerging treatments, including immunotherapy and molecular-targeted agents, could lead to significant advancements in patient care.

Conclusion

Thus, early diagnosis and prompt treatment are crucial for improving clinical outcomes in patients with SCL. Dermatologists play a pivotal role in recognizing these conditions, as they are often the first healthcare professionals to evaluate such lesions and initiate a multidisciplinary approach to patient management.

Conflicts of Interest

The authors have carried out the work on their own and the ICMJE form for Disclosure of Potential Conflicts of Interest have been submitted and none were declared.

References

1. Liu KL, Tsai WC, Lee CH. Non-mycosis fungoides cutaneous lymphomas in a referral center in Taiwan: a retrospective case series and literature review. Plos One. 2020;15(1):e0228046.
2. Lee WJ, Won KH, Won CH, Chang SE, Choi JH, Moon KC, et al. Secondary cutaneous lymphoma: comparative clinical features and survival outcome analysis of 106 cases according to lymphoma cell lineage. Br J Dermatol. 2015;173:134-45.
3. WHO Classification of Tumours Editorial Board. Haematolymphoid tumours. Lyon (France): International Agency for Research on Cancer; Forthcoming 2024. (WHO classification of tumours series, 5th Ed.; Vol. 11). [Last accessed on: February 28, 2025] https://bra01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fpublications.iarc.who.int%2F&data=05%7C02%7C%7C1afb689c54994b6aadae08dd4375d535%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C638740895561085782%7CUnknown%7CTWFpbGZsb3d8eyJFbXB0eU1hcGkiOnRydWUsIlYiOiIwLjAuMDAwMCIsIlAiOiJXaW4zMiIsIkFOIjoiTWFpbCIsIldUIjoyfQ%3D%3D%7C0%7C%7C%7C&sdata=ZyK46UYSj0fxiNcSaS5qHg56OlZjMNRWS9zsdqjHarA%3D&reserved=0
4. Kaddis N, Fisher D, Jacobsen ED. Cutaneous involvement of hematologic malignancies. Hematol Oncol Clin N Am. 2019;33:163-72.
5. Chan JKC, Kwong YL. Common misdiagnoses in lymphomas and avoidance strategies. Lancet Oncol. 2010;11:579-88
6. Qualls G, Salles G. Optimizing CAR T cell therapy in lymphoma. Hematol Oncol. 2021;39:104-12.
7. Matsuki E, Younes A. Checkpoint inhibitors and other immune therapies for Hodgkin and non-Hodgkin lymphoma. Curr Treat Options Oncol. 2016;17:31.
8. Horwitz SM, Ansell S, Ai WZ. T-cell lymphomas, version 2.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2022;20(3):285-308.
9. Liu W, Wu J, Ming X. The utilization of crizotinib and brentuximab vedotin as a bridge to autologous stem cell transplantation and followed by CD30-directed CAR-T cell therapy in relapsed/refractory ALK+ ALCL. Front Immunol. 2024;15:1346001.
10. Agrusa JE, Egress ER, Lowe EJ. Brentuximab vedotin use in pediatric anaplastic large cell lymphoma. Front Immunol. 2023;14:1203471.
11. Hapgood G, Savage KJ. The biology and management of systemic anaplastic large cell lymphoma. Blood. 2015;126(1):17-25.
12. Savage KJ, Harris NL, Vose JM. ALK- anaplastic large-cell lymphoma is clinically and immunophenotypically different from both ALK+ ALCL and peripheral T-cell lymphoma, not otherwise specified: report from the International Peripheral T-Cell Lymphoma Project. Blood. 2008;111(12):5496-504.