Case Report

Leukemia cutis in T-cell acute lymphoblastic leukemia: a 3-year follow-up case report

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Background: Leukemia cutis (LC) is the infiltration of neoplastic leukocytes in the skin that can be observed in various types of leukemia including chronic lymphocytic leukemia, acute myeloid leukemia, and, occasionally, acute lymphoblastic leukemia. LC is considered an unfavorable prognostic factor in previous studies, and most patients die within 1 year after diagnosis. Herein, we report an uncommon case in which a patient presented with LC as the initial symptom of T-cell acute lymphoblastic leukemia (T-ALL) and remained in excellent clinical condition during a 3-year follow-up after treatment.

Case Description: A 50-year-old Chinese woman manifested with multiple infiltrated purplish plaques and tumors over the face, trunk, and lower extremities for more than 5 months, accompanied by recurrent fever and arthralgia. The diagnosis of T-ALL with LC was established by skin biopsy and bone marrow examination. After treatment with chemotherapy and allogeneic stem cell transplantation, the patient achieved complete remission and remained in good health for 3 years. To our knowledge, this is the first described case of a favorable evolution after a 3-year follow-up.

Conclusions: Although uncommon, LC can be the first indication of the presence of T-ALL. This case highlights that early recognition of possible LC and access to treatment may benefit future patients with T-ALL and improve the prognosis of this aggressive disorder.

Keywords: Leukemia cutis (LC); T-cell acute lymphoblastic leukemia (T-ALL); prognosis; case report

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Introduction

Leukemia cutis (LC) is an extramedullary manifestation of leukemia which refers to the cutaneous infiltration of neoplastic leukocytes. LC can be observed in various types of leukemia including chronic lymphocytic leukemia, acute myeloid leukemia, and, occasionally, acute lymphoblastic leukemia (1,2). Herein, we report a case of a female patient with T-cell acute lymphoblastic leukemia (T-ALL) who presented with LC and was in excellent clinical condition during a 3-year follow-up after treatment with chemotherapy and allogeneic stem cell transplantation. We present the following case in accordance with the CARE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-665/rc).

Case presentation

A 50-year-old Chinese woman presented with multiple

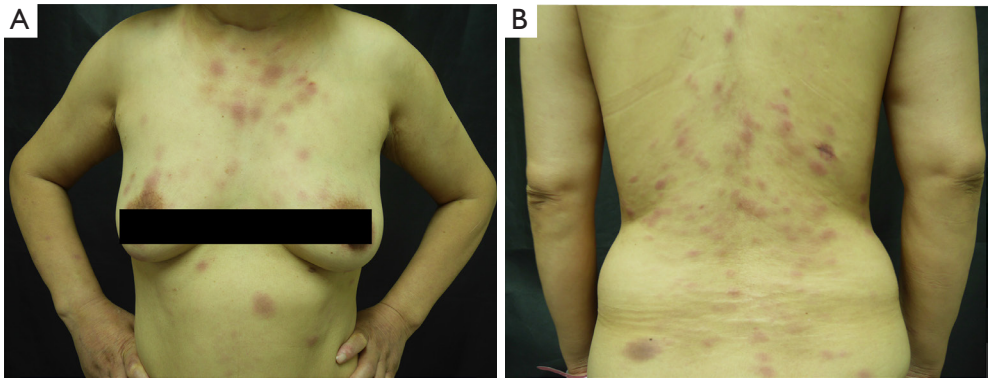

Figure 1 Clinical images of skin lesions. Multiple infiltrated plaques and tumors in the sternal region (A) and back (B). These images are published with the patient's consent.

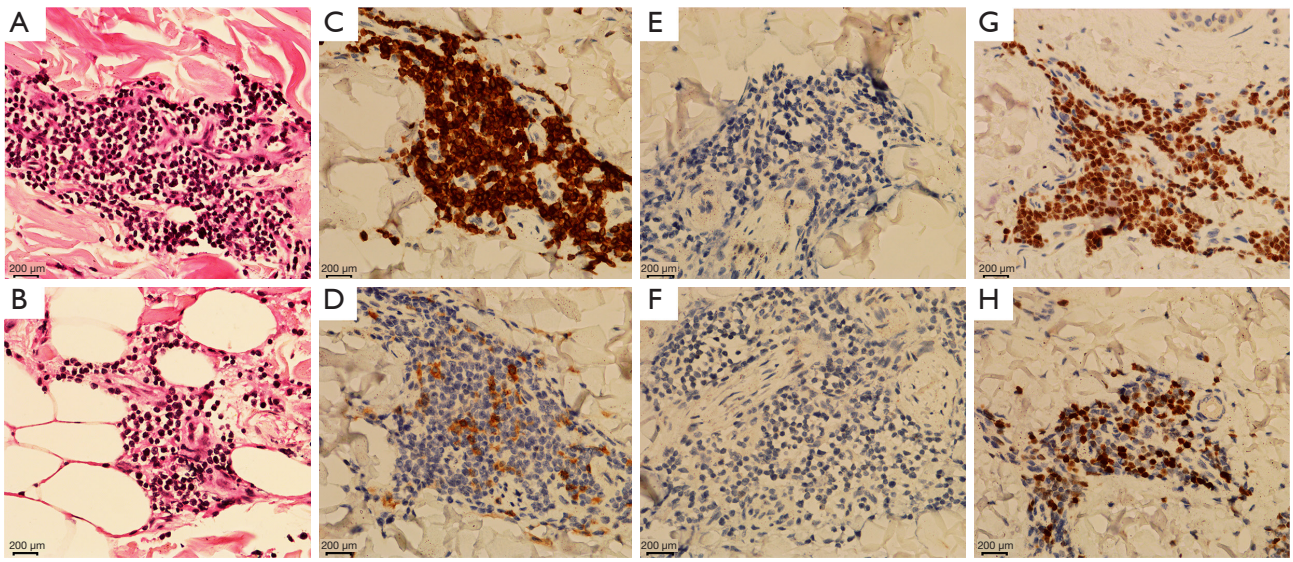

Figure 2 HE staining and immunohistochemistry in skin biopsy. HE staining of skin biopsy showing a dense perivascular and interstitial infiltrate in the dermis and subcutaneous tissue composed of monomorphic atypical cells (A,B). Positive staining of tumor infiltrate for CD3 (C); partial positive staining of tumor infiltrate for CD4 (D); negative staining of tumor infiltrate for CD20 (E) and CD79a (F); strong nuclear positive staining of TdT in the neoplastic cells (G); nuclear staining of the Ki-67 in about 50% of tumor cells (H) (A-H: ×200). TdT, terminal deoxynucleotidyl transferase.

infiltrated purplish plaques and tumors over the face, trunk, and lower extremities for more than 5 months (*Figure 1*), accompanied by recurrent fever and arthralgia. On general examination, we noticed bilateral palpable superficial lymph nodes in the axillary, cervical, and inguinal areas. The patient had a history of latent tuberculosis infection and had been taking the anti-tuberculosis drugs isoniazid and rifapentine. A skin biopsy from lesions in the sternal region showed a dense perivascular dermal and subcutaneous infiltrate composed of monomorphic cells (*Figure 2A*,*2B*). The medium-sized tumoral cells showed scant cytoplasm and a circular or irregular prominent nucleus with fine chromatin and inconspicuous nucleoli. The epidermis was uninvolved. Tumor lymphocytes were positive for CD3, partial CD4, partial CD10, CD7, LMO2, and terminal deoxynucleotidyl transferase (TdT), and negative for CD20, CD79a, CD1a, CD56, CD34, CD2, CD30, MPO, and CD117 (*Figure 2C-2G*). A high proliferative index

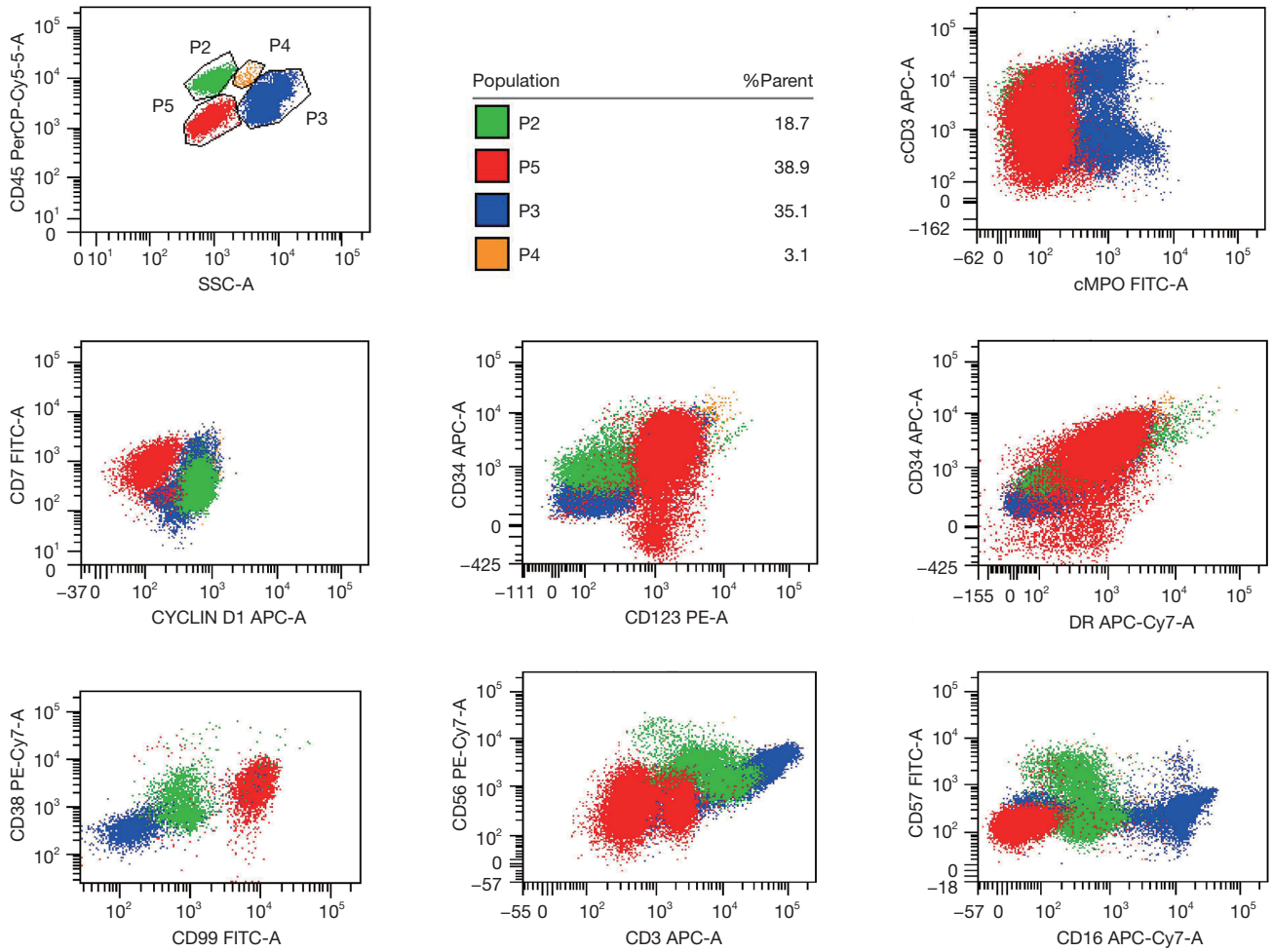

Figure 3 Flow cytometric immunophenotyping graphs of the marrow. Blasts (P5) are shown in red, lymphocyte (P2) in green, granulocyte (P3) in blue, and monocyte (P4) in yellow. Blasts are positive for cCD3, CD7, CD123, CD34, CD38, HLA-DR, CD99 and negative for CD56 and CD16.

(Ki67≈50%) was observed in the tumoral cells (*Figure 2H*), revealing the possible presence of lymphoblastic neoplasms. Anemia was notably discovered in the laboratory investigation, with a hemoglobin level of 10.5 g/Dl. Laboratory findings further revealed an increased percentage of lymphocytes in the peripheral blood (68.6%) and an elevated erythrocyte sedimentation rate (70 mm/h). Bone marrow smear examination indicated 85.5% abnormal lymphocytes, which were described as having dispersed chromatin, light blue-staining cytoplasm, and large nuclei in most cells. Flow cytometry revealed that these atypical cells expressed cCD3, CD7, CD123, CD34, CD38, HLA-DR, and CD99, and did not express CD56 and CD16 (*Figure 3*). Molecular studies were negative for BCR-ABL fusion and MLL rearrangement. High CRLF2 expression and TERF2-Jak2 mutation were detected, which are usually identified in patients with high-risk T-ALL (3). Chromosomal analysis indicated 46, XX[9]. Positron emission tomography-computed tomography (PET-CT) results indicated glycolytic hypermetabolism in the cervical and bilateral supraclavicular lymph nodes, thymus gland, and spleen, as well as in the skin tumors of the trunk and lower extremities. The result of cerebrospinal fluid testing to investigate the involvement of the central nervous system was negative. The patient was ultimately diagnosed with T-ALL. She was subsequently referred to the department of hematology, where she was admitted for treatment with a VDLD regimen (vindesine, 4 mg/week ×4; daunorubicin

40 mg/m^2/day ×3; L-asparaginase, 3,750 U/week ×2; dexamethasone, 10 mg/m^2/day ×14) and allogeneic stem cell transplantation. No severe adverse events that could lead to the termination of treatment occurred. On the 10th day of chemotherapy, the skin lesions nearly disappeared. The patient was extremely satisfied with the treatment. She subsequently achieved a complete response and has not had disease recurrence in 3 years.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

LC involves the infiltration of neoplastic leukocytes in the skin. The sequence of the appearance of LC and the diagnosis of underlying leukemia varies. Most patients present with LC after leukemia has already been diagnosed or concurrently with systemic leukemia. On several occasions, skin involvement—which affects up to 7% of patients with leukemia—may precede bone marrow or peripheral blood involvement by several months or years (1). Importantly, LC may further signal the early relapse of leukemia (4).

The most common clinical lesions in LC present as papules, nodules, infiltrated plaques, and larger tumors that may be distributed over the scalp, face, trunk, and extremities (5). Nearly all skin lesions present with a purple or red appearance without obvious accompanying subjective symptoms such as pruritus and pain. Despite the characteristic clinical manifestations of LC, its diagnosis predominantly depends on histopathological features including the pattern of distribution, morphology, and immunophenotype of tumor cells. In T-ALL, a dense and diffuse monotonous infiltrate of medium-sized lymphoid cells appears in the dermis and even in the subcutaneous tissue. The epidermis is uninvolved, potentially differentiating primary cutaneous T-cell lymphoma. Tumor cells typically display T lineage-specific markers such as CD3, CD4, or CD8 and an immature T-cell phenotype including positive staining for one or more precursor markers such as TdT, CD99, CD34, and CD1a (1,4,6). Most notably, TdT shows higher sensitivity than CD99, CD34, and CD1a. Before making the ultimate diagnosis, both hematologic findings from the peripheral blood and bone marrow and the results of PET-CT should be considered. Additionally, as our patient presented with skin lesions as the initial symptom and the lymph nodes and bone marrow were subsequently found to be involved, other tumors with similar manifestations—such as blastic plasmacytoid dendritic cell neoplasm—should be excluded. The tumor cells in blastic plasmacytoid dendritic cell neoplasm are usually monomorphic, poorly differentiated, and intermediate-sized blasts with fine chromatin, which most importantly express CD4, CD56, and CD123 (7).

Although a few cases of LC in T-ALL were reported in the literature from 1999 to 2021 (4,6,8-11), only one neonate has been described with a follow-up of 2 years after treatment, and no detailed records of treatment and follow-up in adult patients have been found (11). This case is the first described with a favorable evolution after a 3-year follow-up. LC is considered an unfavorable prognostic factor in most situations. A recent study from the United States has shown that more than 80% of patients with LC patients die within one 1 year of diagnosis (12), and another international study indicated that the median survival time of patients with LC is 7.2 months (5). Furthermore, elevated CRLF2 expression is proven to be associated with poor outcomes in children and adults (3). Despite the evidence suggesting a poor prognosis, we describe a rare case where the patient with LC maintained good health for 3 years after receiving the combination of chemotherapy and allogeneic stem cell transplantation.

In summary, although uncommon, LC can be the first indication of the presence of T-ALL. Clinicians should consider the possibility of LC when skin lesions appear as multiple purplish red nodules, infiltrated plaques, or larger tumors without additional symptoms. Early identification of LC may allow for more rapid initiation of treatment and thus improved prognosis.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-665/rc

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-665/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-665/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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