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Bullous leukemia cutis in a patient with T-cell prolymphocytic leukemia



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Leukemia cutis (LC) is a rare, cutaneous infiltration of neoplastic leukemic cells and correlates strongly to additional sites of extramedullary disease.¹ LC is a nonspecific term for the cutaneous manifestations of many subtypes of leukemia; therefore, the cutaneous morphology and histopathology of LC varies widely. This distinction makes it clinically difficult to distinguish from other nonspecific lesions, especially in the bullous subtype, which is rare and clinically mimics bug bites.² LC usually follows or occurs concomitantly with the diagnosis of leukemia, and its presence is an indicator of poor prognosis.¹ Proper diagnosis of LC is essential because it can alter a patient's treatment course.

CASE PRESENTATION

A 47-year-old African-American man with recently diagnosed T-cell prolymphocytic leukemia (T-PLL) presented in the clinic with a widespread rash for 2 and a half weeks. Nine months before the dermatology clinic visit, he was admitted to the hospital with a 2-month history of fatigue, abdominal discomfort, a white blood cell count of greater than 150K, and generalized lymphadenopathy. Pathology of an excisional lymph node biopsy found extensive infiltration by atypical CD2⁺, CD3⁺, CD5⁺, CD7⁺, CD8⁺, and TCL-1⁺ T cells, indicative of T-PLL. Fluorescence in situ hybridization analysis found trisomy 8 and a *TCRAD* gene rearrangement involving 14q11. Bone marrow biopsy found 85% bone marrow involvement. He has since been treated with alemtuzumab and pentostatin. Besides

Abbreviations used:

LC: leukemia cutis
T-PLL: T-cell prolymphocytic leukemia

the diagnosis of leukemia, his medical history was unremarkable.

On physical examination, there were multiple skin-colored, violaceous to red-brown papules and nodules on the entire body including the groin area, with central vesicles or tiny, crusted erosions (Fig 1, A). A skin biopsy specimen found marked spongiosis and edema of the papillary dermis with perivascular infiltrate of atypical lymphocytes in the papillary and reticular dermis (Fig 1, B and C).

Most of the atypical lymphocytes stained positively for CD3, CD5, CD7, and CD8, consistent with previous biopsy results of the lymph node, peripheral blood, and bone marrow, confirming the presence of leukemia cells. Thus, a definitive diagnosis was made for LC secondary to the patient's known T-PLL.

DISCUSSION

T-PLL has an aggressive course and is rare, representing about 2% of mature lymphocytic leukemias in adults older than 30.³ The outcome for these patients is poor, even without cutaneous involvement.¹ LC is seen in 25% to 30% of cases of T-PLL.² Frequency of LC varies widely depending on the subtype of leukemia and is much higher in children than in adults (Table 1). Skin lesions in LC

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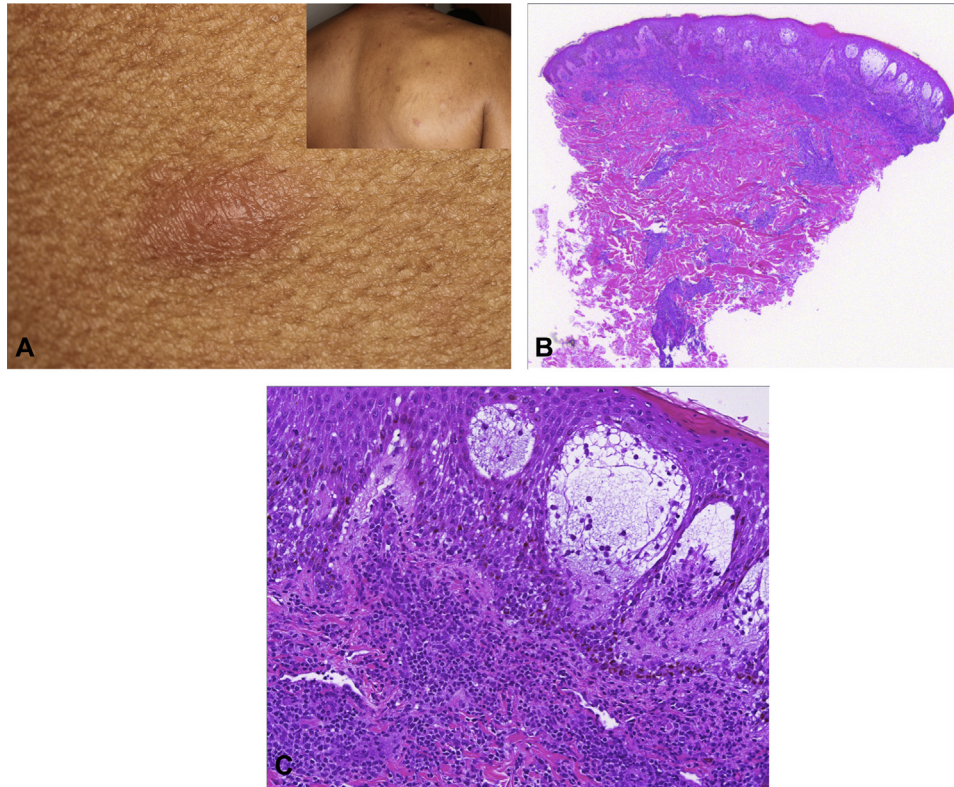


Fig 1. **A**, Multiple, widespread variably sized red-brown papules or nodules with central vesicles or erosions in a patient with T-PLL. **B** and **C**, Within the superficial and deep dermis there is a perivascular infiltrate of atypical lymphocytes. There is marked spongiosis and edema of the papillary dermis.

can be single or multiple, violaceous, red-brown, or hemorrhagic papules, nodules, and plaques of various sizes. Erythematous nodules and papules are the most common clinical presentation. Legs are most commonly involved, followed by arms, back, chest, scalp, and face.² In T-PLL patients, LC can manifest as a maculopapular rash, skin nodules, and occasionally erythroderma.⁴ Petechial or purpuric qualities can be noted because of red blood cell extravasation. Vesiculobullous eruptions are rarely observed in LC. They were observed in one of 75 Korean patients with LC, 2 of 42 LC cases reviewed by the Mayo Clinic, and none in 26 patients with cutaneous myeloid leukemia.⁵⁻⁷ Clinical differential diagnoses include septic emboli, vasculitis, lymphoma cutis, bug bites, and drug eruptions.⁸

Diagnosis of LC is based on several factors including morphology of skin infiltration, cytology, and immunohistochemistry. Most leukemic skin infiltrates have a perivascular or periadnexal pattern. A dense diffuse/interstitial or nodular infiltrate involving the dermis and subcutis with sparing of the upper papillary dermis can also be seen.² Skin infiltrates in T-PLL are primarily in the upper dermis with perivascular and periadnexal distribution.⁴

There is no epidermotropism, differentiating it from mycosis fungoides.² Combined with the patient's history of T-PLL, the histopathologic and immunophenotypic findings in the cutaneous biopsies favor bullous LC. Thus, other differentials were ruled out, and a diagnosis of cutaneous involvement by the patient's known T-PLL was made.

T prolymphocytes are peripheral T cells that are CD2⁺, CD3⁺, CD7⁺, and CD52⁺, resulting in similar immunostaining of cutaneous biopsies of LC⁺ T-PLL patients.³ Most T-PLL infiltrates are CD4⁺/CD8⁻, but 13% are CD4⁻/CD8⁺, as seen in this patient.² T-cell leukemia-1 (TCL-1) oncogene immunostaining in neoplasms of known T-cell lineage is also specific to T-PLL, and high expression is a poor prognostic marker.⁴ In T-PLL, the most frequent chromosome abnormality involves an inversion of chromosome 14 with breakpoints at q11 and q32, seen as a *TCRAD* gene rearrangement (14q11) in this patient.³ Trisomy 8 is also seen in two-thirds of T-PLL cases.⁹ This patient had morphologic, phenotypic (positive T-cell markers and TCL-1 oncogene), and cytogenetic (trisomy 8 and *TCRAD* gene rearrangement) findings consistent with LC related to systemic T-PLL. Bullae formation is speculated to result from lymphatic obstruction,

Table I. Subtypes of leukemia with skin involvement

Subtypes	Frequency of skin involvement
Myeloid/monocytic	
Acute myeloid leukemia	10%–15%
Acute myelomonocytic leukemia	Up to 50%
Acute monocytic leukemia	Up to 50%
Chronic myelogenous leukemia	<10%
Chronic myelomonocytic leukemia (transformation)	<10%
Myelodysplastic syndromes (transformation)	<10%
Lymphoproliferative disorders	
B-cell leukemias/lymphomas	
Precursor B-cell acute lymphoblastic leukemia	Unusual
Chronic lymphocytic leukemia/small lymphocytic lymphoma	4%–20%
T-cell leukemias/lymphomas	
Precursor T-cell acute lymphoblastic leukemia	Unusual
Adult T-cell leukemia/lymphoma	43%–72%
T-cell prolymphocytic leukemia	25%–30%
Sézary syndrome	20%–70%

Data from Cho-Vega, JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. *Am J Clin Pathol* 2008;129(1):130-142.

vascular occlusion, extensive upper dermal edema, or injury at the dermoepidermal junction.¹⁰

Studies find that 88% of patients who have LC die within 1 year of diagnosis. The prognosis of bullous LC is unknown because of limited number of cases. Because LC is a cutaneous manifestation of a systemic disease, treatment should be aimed at the systemic disease with intensive chemotherapy and hematopoietic stem cell transplantation, as well as local symptoms.² Currently, intravenous alemtuzumab (anti-CD52) is the best treatment for T-PLL, with more than 90% response rates and significant improvement in survival.³

LC related to T-PLL has also been found to respond well to alemtuzumab therapy. Autologous or allogeneic stem cell transplant after remission further prolongs survival, with the latter as a

potential cure.⁴ In this case, although the patient's brother is a haplo match, the patient is waiting for his disease to be further controlled on alemtuzumab and pentostatin before stem cell transplantation.

T-PLL is a rare and aggressive hematologic malignancy. Although the skin is characteristically involved, it is not a well-recognized entity in dermatologic literature, especially the subtype of bullous LC. LC can often be the manifestation of a leukemia relapse. A diagnosis of LC generally portends a poor prognosis and strongly correlates with additional sites of extramedullary involvement. Accurate diagnosis has tremendous prognostic importance and can significantly alter the treatment regimen of patients. This case report has key clinical implications in bringing awareness to this disease, leading to prompt diagnosis and better treatment of affected patients.

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