Leukemia cutis mimicking tumid lupus as the presenting sign in a case of mixed T/B-cell acute lymphoblastic leukemia

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INTRODUCTION

Leukemia cutis (LC) is rare and can have varying clinical and histopathologic presentations.[1,2] In acute lymphoblastic leukemia (ALL), LC has been reported in 1% to 3% of cases and usually after diagnosis, although it can present simultaneously, or even precede, the diagnosis of leukemia.[3-5] The clinical appearance of the leukemic infiltrate in the skin typically includes papules, plaques, and nodules and infrequently has mimicked inflammatory disorders.[1,3,6,7] Uncommonly, LC also mimics inflammatory disorders histopathologically, with a sparse perivascular or interstitial infiltrate instead of more dense nodular infiltrates.[1,8] Immunohistochemistry can be helpful in differentiating malignant versus inflammatory cell infiltrates.[8-11] Diagnosis may be delayed in these less common presentations of LC with an inflammatory pattern, particularly without a prior history of leukemia. Maintaining a high level of suspicion for LC in addition to appropriate utilization of immunohistochemical stains can be highly valuable in the diagnostic workup of patients with either known leukemia or systemic signs or symptoms concerning for leukemia.

CASE REPORT

A 34-year-old previously healthy woman was evaluated for an asymptomatic rash on the face, chest, abdomen, back, and arms for 2 months before hospital admission for symptomatic anemia with a hemoglobin level of 7.3 g/dL requiring red blood cell transfusion. Her white blood cell count was low at 3,400 cells/μL, and she had thrombocytopenia with platelets at 104,000/μL. Hepatic enzymes and lactate dehydrogenase were within normal limits. She also experienced cough, fatigue, and unintentional weight loss during these 2 months. A short course of oral corticosteroids failed to improve findings. Punch biopsy on the abdomen was performed 3 weeks before hospital admission and found a perivascular lymphocytic infiltrate. She did not have a history of an inciting insult such as a burn, radiation, or known inflammatory dermatosis before development of the rash. She had no family history of autoimmune disease, and her family history was notable only for breast cancer in her aunt.

Physical examination found pink infiltrated dermal papules and plaques without epidermal change on her forehead, chin, chest, abdomen, back, arms, and malar cheeks with sparing of the nasolabial folds (Fig 1). She also had prominent cervical and supraclavicular lymphadenopathy. There was no oral mucosal involvement. The differential diagnosis included inflammatory autoimmune disorders such as tumid lupus erythematosus and systemic lupus erythematosus as well as LC given her

Abbreviations used:

ALL: acute lymphoblastic leukemia
LC: leukemia cutis
TdT: terminal deoxynucleotidyl transferase

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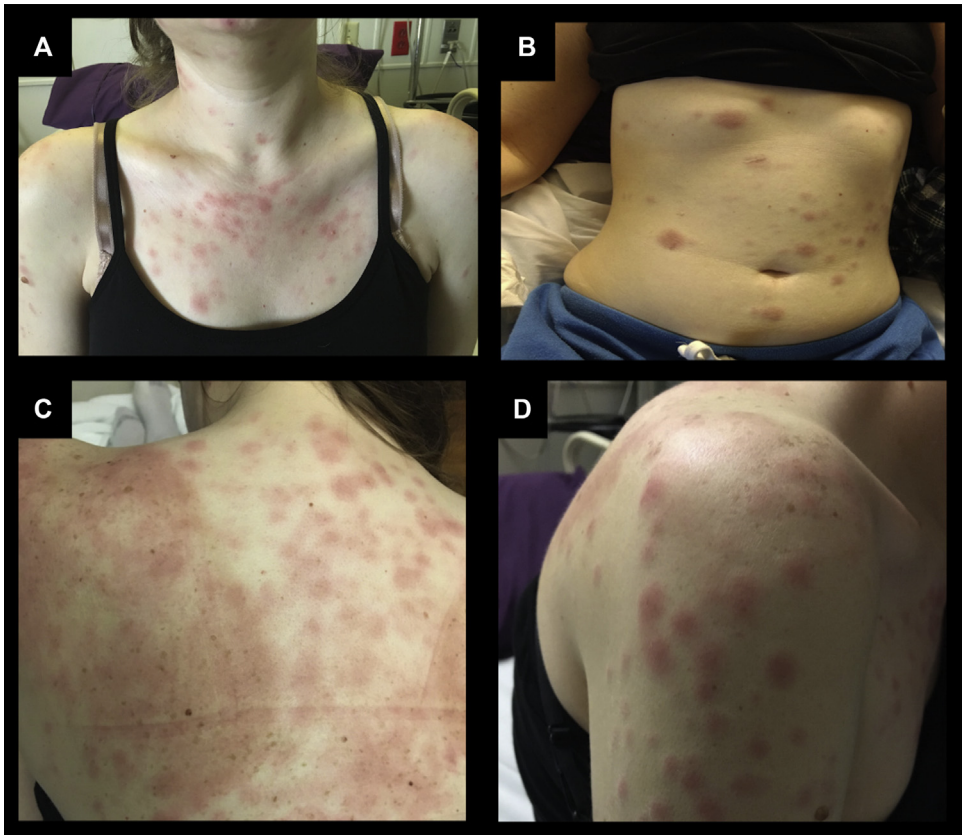

Fig 1. Pink papules and plaques located on **A**, chest; **B**, abdomen; **C**, back; and **D**, upper arm on initial presentation.

unintentional weight loss and notable lymphadenopathy. Computed tomography was ordered because of the physical examination findings of lymphadenopathy and found mildly enlarged cervical, axillary, mediastinal, and supraclavicular lymphadenopathy and splenomegaly. Chest radiograph showed no pulmonary findings. Skin biopsies were taken of this rash from her left upper back and left upper arm. At scanning magnification, histopathology showed a perivascular and periadnexal lymphocytic infiltrate mimicking tumid lupus (Fig 2) However, there was a lack of mucin or plasmacellular infiltrates that are typical of tumid lupus erythematosus. Furthermore, the lymphocytic infiltrate was composed of monomorphous medium-sized cells with prominent nuclei and increased nuclear/cytoplasmic ratios, representative of an atypical lymphoid infiltrate composed of blasts. Angioimmunoblastic T-cell lymphoma was considered given patient's clinical presentation and systemic symptoms, but this diagnosis was not favored given the lack of vascular proliferation and paucity of plasma cells, histiocytes, and eosinophils. Lymphoblasts were immunopositive for CD3, CD5, CD7, CD79a, and terminal deoxynucleotidyl transferase (TdT), whereas CD20 was negative (Fig 3). Peripheral blood smear found lymphoblasts, with peripheral blood flow cytometry identifying 43% lymphoblasts. Flow cytometry of skin showed 70% lymphoblasts of mixed T/B-cell lineage, consistent with mixed T/B-cell ALL, which was confirmed by bone marrow biopsy. The bone marrow aspiration showed 85% lymphoblasts, and fluorescence in situ hybridization was negative for clonal aberrations. The karyotype was normal (46, XX). CD45 and side light scatter were used to identify the blast population, and detected 82% blast cells, with bright CD7 expression and lacking CD4 and CD8 expression. Coexpression of CD19 was detected. There was no significant expression of CD20 or CD10. The blasts were negative for myeloid markers. Lastly, serologic evaluation for lupus erythematosus, including antinuclear antibodies, SS-A Ab, SS-B Ab, and dsDNA Ab, was negative.

The patient was started on augmented hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) chemotherapy. In the ensuing weeks, the papules and plaques became visibly less

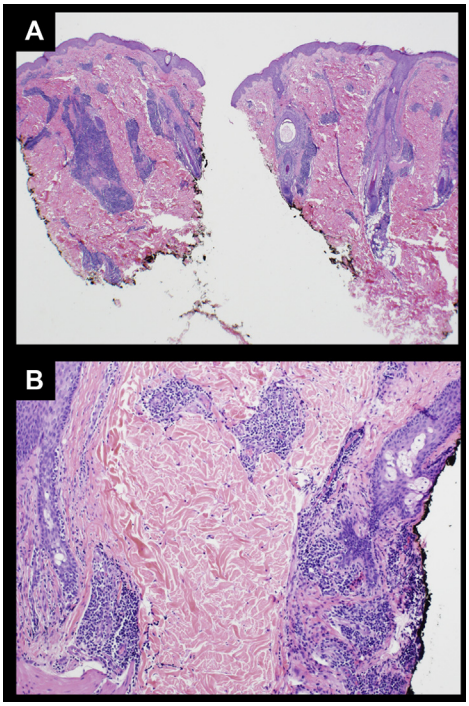

Fig 2. **A**, Superficial and deep perivascular and periadnexal lymphoid infiltrate. **B**, Monomorphous mononuclear cells surround adnexal structures. Medium-size cells with prominent nuclei and increased nuclear/cytoplasmic ratios. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×20; **B**, ×200.)

infiltrative and faded in color (Fig 4). The dermatology department followed up with her for 16 days during her hospital admission. After completing 4 cycles of chemotherapy followed by haploidentical bone marrow transplant several months after admission, she was in complete remission. Cutaneous findings did not recur as of 6 months following diagnosis.

DISCUSSION

LC is most commonly diagnosed in patients with known leukemia. However, LC may develop concurrently with other manifestations of acute leukemia or even precede the clinical detection of leukemia.[1,2] Because the clinical findings of LC are variable, histopathologic evaluation is essential for diagnosis. There are only rare reports of LC mimicking lupus erythematosus. One case of LC in the setting of acute myelogenous leukemia presented with facial erythema simulating a butterfly rash,[6] and another case of ALL in a child presented with erythematous macules on the cheeks.[7] Both diagnoses of LC were confirmed by histopathology.

The morphology and distribution of the patient's rash—with erythematous dermal plaques more prominently on sun-exposed areas of the cheeks, chest, upper back, and upper arm—simulated cutaneous lupus erythematosus, in particular, tumid lupus. This distribution was unique based on a review of the literature. A high suspicion for LC, because of associated signs of prominent lymphadenopathy and unintentional weight loss, led to further diagnostic evaluation including immunohistochemistry and flow cytometry.

A perivascular and periadnexal pattern of LC has been described,[8-10] and this inflammatory pattern may delay diagnosis, particularly when the inflammation is sparse. For very rare cases that simulate lupus both clinically and histopathologically, several features can be helpful in prompting an immunohistochemical evaluation. Specifically, an absence of mucin, plasma cell infiltrate, and vacuolar change points away from a diagnosis of lupus and, in the right clinical setting, supports the use of immunohistochemistry for further workup. Immunohistochemical stains are helpful in identifying premature malignant cells in the infiltrate. Common immunohistochemical markers that are usually positive for T-cell ALL include CD3, CD5, and TdT. CD79a, as well as TdT, are frequently positive in B-cell ALL. In mixed T/B-cell acute lymphoid leukemia, CD3, CD5, CD7, CD79a, and TdT are positive. Mixed phenotype acute leukemia is rare, accounting for less than 4% of all acute leukemias.[12] Among cases of mixed phenotype acute leukemia, the myeloid/B-cell type is most frequently observed.[12] For the patient described here, immunophenotyping showing both T- and B-cell features in ALL is particularly rare.[12]

LC must be differentiated from nonspecific cutaneous manifestations of the underlying malignancy.[1,3,8] Because her bone marrow was predominantly composed of malignant cells at the time of diagnosis and the autoimmune workup was negative, the malignant infiltrate in her skin is not felt to be an inflammatory process with incidental malignant cells secondary to her acute leukemia. Her rash clinically improved during the first several weeks of induction chemotherapy, consistent with literature reports of LC improving during treatment of the underlying leukemia.[7]

We present a rare case of cutaneous leukemic infiltrate mimicking tumid lupus erythematosus in a patient who concurrently had mixed T/B-cell ALL. Our case highlights the value of clinicopathologic correlation, which can be an important guide when additional workup is warranted, including immunohistochemistry.

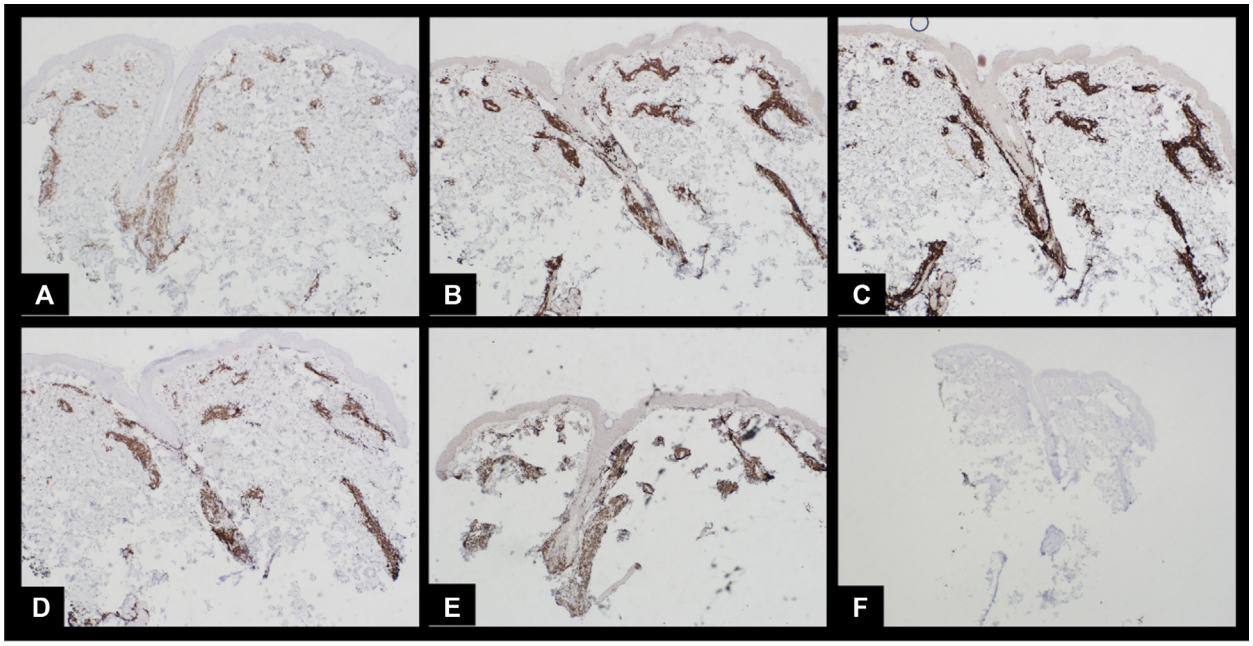

Fig 3. Immunohistochemical stains show positivity for **A**, CD3; **B**, CD5; **C**, CD7; **D**, CD79a; and **E**, TdT and **F**, negativity for CD20. This immunophenotype matched that of the bone marrow biopsy specimen consistent with mixed T- and B-cell lineage ALL. (Original magnifications: **A**-**E**, ×40; **F**, ×20.)

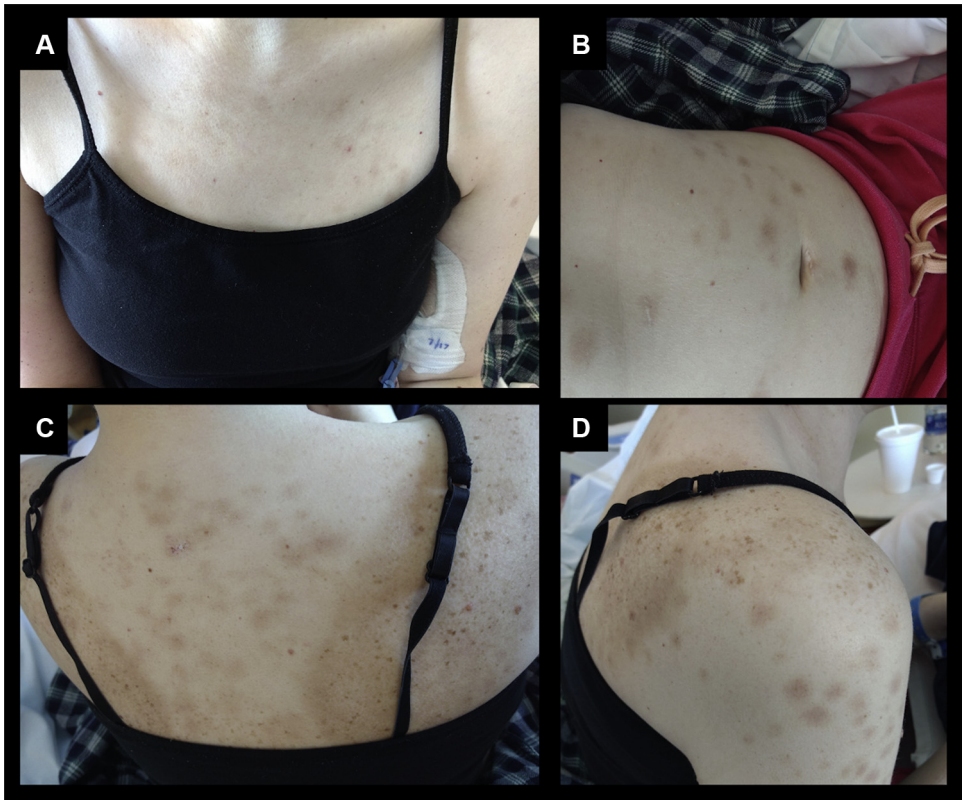

Fig 4. Cutaneous leukemic papules and plaques faded after several weeks of induction chemotherapy: chest (**A**), abdomen (**B**), back (**C**), and shoulder (**D**).

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