Leukemia Cutis of the Nose

Madeliene Gainers, MD; Rana Rofagha, MD; Joseph C. English III, MD

Leukemia cutis (LC) represents metastatic spread of aggressive systemic leukemia to the skin and heralds a poor prognosis. We report a patient with a history of chronic lymphocytic leukemia presenting as a recalcitrant nasal cellulitis that proved to be involved by LC on skin biopsy. As demonstrated by this case, LC can mimic inflammatory dermatoses, resulting in failure of an accurate diagnosis and consequently inappropriate treatment and delay in optimal therapy. In patients with a history of leukemia, histopathologic examination of refractory conditions is essential and should be performed early in the treatment strategy.

Cutis. 2007;80:208-210.

Case Report

A 51-year-old man with a history of chronic lymphocytic leukemia was admitted to a tertiary care center because of presumed nasal cellulitis recalcitrant to 12 weeks of intravenous antibiotics administered at home. Aside from the erythematous indurated papules and plaques on the patient's central face, his physical examination was unremarkable. The lesions were not exudative or warm. Laboratory examinations revealed anemia at 8 g/dL for hemoglobin (reference range, 14–17 g/dL), an elevated white blood cell count of 34,000 cells/dL (reference range, 4.8–10.8 K/μL or 4800–10,800 cells/dL) with absolute neutropenia, and severe thrombocytopenia (<10,000 cells/dL; reference range, 130,000–460,000 cells/dL). Tagged white blood cell scan showed increased uptake in the nose, and computed tomographic scans were interpreted as sinusitis.

Progressive nasal induration and development of necrotic eschar raised the possibility of mucormycosis, and aggressive systemic antifungal therapy was initiated. Continued lack of clinical response prompted dermatologic consultation (Figure 1). A biopsy revealed pseudoepitheliomatous hyperplasia with associated necrosis and heterogeneous infiltrate of small lymphocytes, plasma cells, and occasional histiocytes, as well as clusters of large transformed cells with prominent nucleoli. Immunohistochemististry testing revealed positivity for BCL-2, CD20, CD43, and Ki67, with aberrant expression of CD5 (Figures 2 and 3). A pathologic diagnosis of an atypical B-cell lymphoproliferative disorder was made, and a clinical diagnosis of leukemia cutis (LC) consistent with chronic lymphocytic leukemia was rendered.

The patient's antifungal therapy was then discontinued, but broad spectrum antibiotic therapy was continued because of his neutropenia. Chemotherapy was considered but abandoned after the patient's clinical status declined. He was scheduled for local radiation therapy but became septic and all therapy was discontinued. The patient's status was changed to do not resuscitate and he subsequently died.

Comment

LC is the cutaneous metastasis of systemic leukemia and represents a specific lesion of leukemia as neoplastic cells are demonstrated in the skin.[1] These lesions often manifest as erythematous to violaceous papules, nodules, or indurated plaques that have a firm consistency and may involve the epidermis, dermis, or subcutis.[2] Although the presentation is largely nondescript, specific lesions do imitate inflammatory dermatoses. LC has previously been reported to simulate erythema nodosum, mycosis fungoides, pyoderma gangrenosum, guttate psoriasis, scrotal ulcer, and stasis dermatitis.[2-4] Additionally, LC has been known to localize within sites of previous trauma, ulceration, scar, and surgery.[2,5] Nonspecific lesions, also referred to as leukemids, represent infiltration of leukemic cells into inflamed skin, often in the setting of a drug-induced exanthema in patients with leukemia.

Accepted for publication November 16, 2006.

Dr. Gainers is from the Harvard Skin Disease Research Center, Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts. Drs. Rofagha and English are from the University of Pittsburgh Medical Center, Department of Dermatology, Pennsylvania.

The authors report no conflict of interest.
Reprints not available from the authors.

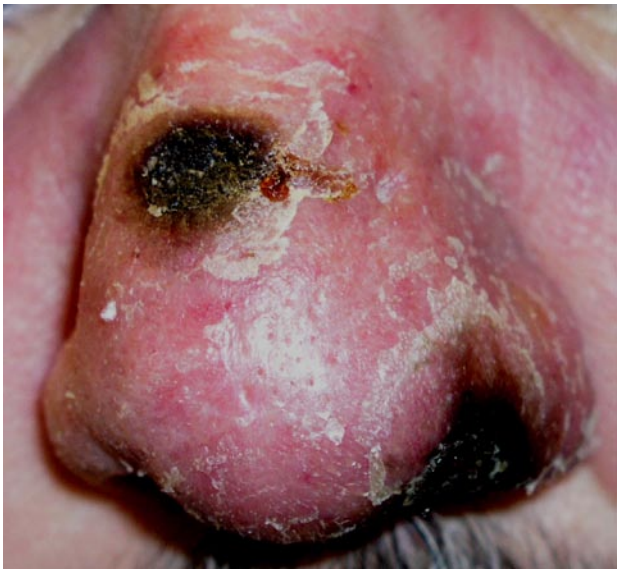

Figure 1. Erythema and necrotic eschar overlying the patient's central face.

Cutaneous injury or inflammation may serve as the initiating factor in recruiting leukemic cells to sites of inflammation. In response to skin trauma, keratinocytes release IL-1, which initiates a cascade of further keratinocyte activation and greater IL-1 production. Other chemotactic agents such as granulocyte colony-stimulating factor, IL-3, and IL-6 also are released.[6,7] These cytokines generate a chemoattractant milieu within the skin for inflammatory cells.[6] In patients with leukemia, the infiltration of inflamed skin by leukemic cells is reflected by the predominance of atypical leukocytes in the blood.

LC represents aggressive disease and heralds a poor prognosis for patients, as more than 80% of patients with LC die within a year of diagnosis.[1,2] Management of this process is a therapeutic challenge because the skin can serve as a protective reservoir of leukemic cells.[2] In addition to systemic chemotherapy to induce bone marrow suppression, treatment must be directed toward the complete elimination of cutaneous infiltrates.[8,9] Thus, entire body electron beam irradiation of the skin, in combination with systemic chemotherapy, is required to offer the patient the greatest chance for remission.[8,10]

Given the rarity of LC, the incidence is not well-described and varies depending on malignancy subtype. For lymphocytic and granulocytic leukemia, the incidence is reported as ranging from 1.3% to 20% compared with 10% to 50% for monocytic leukemia.[6,11] Despite its low incidence, LC should be considered in the differential diagnosis of common inflammatory dermatoses in patients with leukemia recalcitrant to conventional therapies, as it can simulate these processes. Histopathologic examination is essential and should be performed early in the management strategy to deliver the most appropriate and optimal therapy.

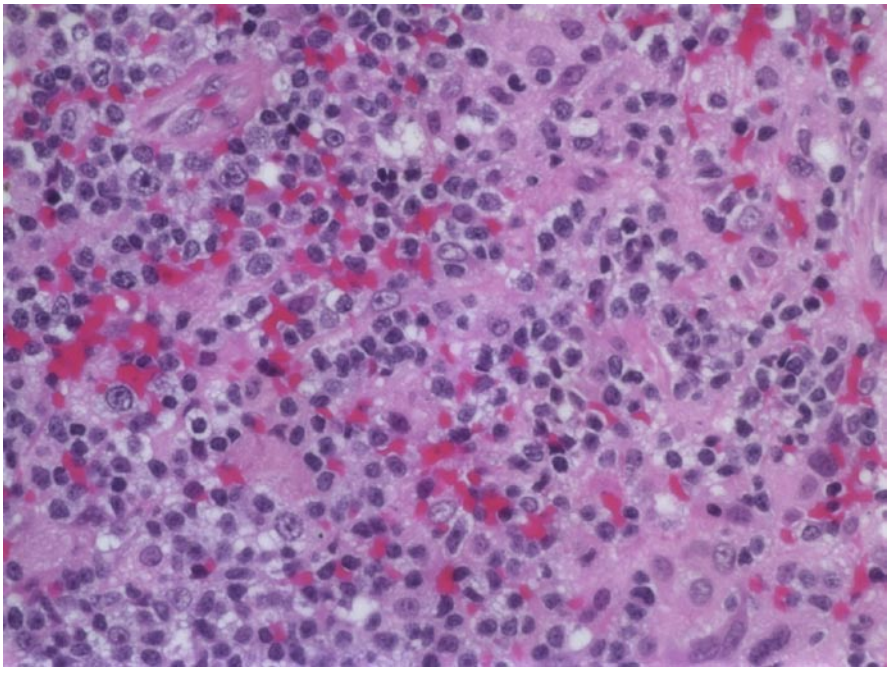

Figure 2. Large atypical cells within an inflammatory infiltrate (H&E, original magnification ×20). Photograph courtesy of Leena T. Lourduraj, MD.

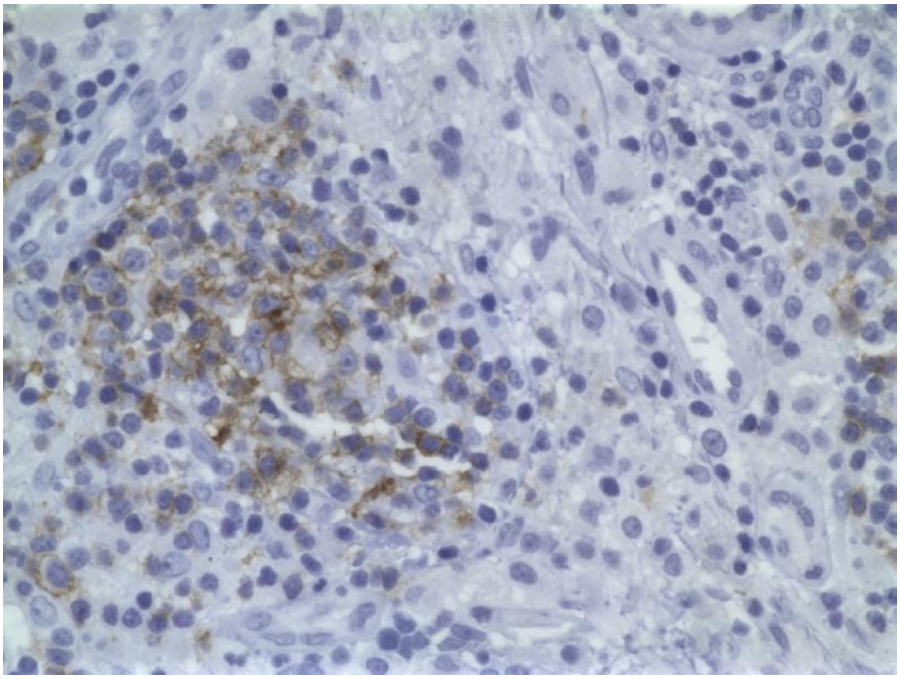

Figure 3. Immunohistochemistry of large atypical cells staining positively for CD20 (original magnification ×20). Photograph courtesy of Leena T. Lourduraj, MD.

REFERENCES

1. Su WP. Clinical, histopathologic, and immunohistochemical correlations in leukemia cutis. *Sem Dermatol*. 1994;13:223-230.
2. Ratnam KV, Khor CJL, Su WPD. Leukemia cutis. *Dermatol Clin*. 1994;12:419-431.
3. Stawiski MA. Skin manifestations of leukemias and lymphomas. *Cutis*. 1978;21:814-818.
4. Zax RH, Kulp-Shorten CL, Callen JP. Leukemia cutis presenting as a scrotal ulcer. *J Am Acad Dermatol*. 1989;21:410-413.
5. Berger BJ, Gross PR, Daniels RB, et al. Leukemia cutis masquerading as guttate psoriasis. *Arch Dermatol*. 1973;108:416-418.
6. Koizumi H, Kumakiri M, Ishizuka M, et al. Leukemia cutis in acute myelomonocytic leukemia: infiltration to minor traumas and scars. *J Dermatol*. 1991;18:281-285.
7. Kupper TS. Mechanisms of cutaneous inflammation. interactions between epidermal cytokines, adhesion molecules, and leukocytes. *Arch Dermatol*. 1989;125:1406-1412.
8. Rubin CM, Arthur DC, Meyers G, et al. Leukemia cutis treated with total skin irradiation. *Cancer*. 1985;55:2649-2652.
9. Haubenstock A, Zalusky R, Ghali VS, et al. Isolated leukemia cutis—a case report. *Am J Hematol*. 1987;24:437-439.
10. Baer MR, Barcos M, Farell H, et al. Acute myelogenous leukemia with leukemia cutis. eighteen cases between 1969 and 1986. *Cancer*. 1989;63:2192-2200.
11. Su WP, Buechner SA, Li CY. Clinicopathologic correlations in leukemia cutis. *J Am Acad Dermatol*. 1984;11:121-128.