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Recurrence Leukemia Cutis in Acute Myeloblastic Leukemia

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We report the case of a 64-year-old female with acute myeloblastic leukemia (French-American-British classification: M2) who developed two specific cutaneous manifestations during her illness. She presented with extensive cellulitis involving the face, neck, and upper chest wall. While the cellulitis resolved with antibiotic therapy, a fungating ulcerated nodule remained on the lower lip which proved to be leukemic on biopsy. Concomitant blood and bone marrow findings were diagnostic of acute myeloblastic leukemia. The lip lesion cleared with a course of chemotherapy. An erythematous macular rash subsequently developed over the lower trunk which was thought to be an allergic reaction to the penicillin treatment. However, biopsy results were consistent with leukemia cutis. A repeat bone marrow examination revealed excessive blasts. Our observations emphasize the various presentations of leukemia cutis and the need to biopsy any cutaneous lesion of unclear etiology in the setting of acute leukemia. (Henry Ford Hosp Med J 1989;37:76-8)

A variety of cutaneous manifestations have been described in association with leukemia. Most of these are nonspecific lesions, such as petechiae, ecchymosis, pyoderma, erythema multiforme, bullous pemphigoid, and hyperpigmentation, as well as nonspecific maculopapular and eczematous eruptions (1). Various bacterial and mycotic skin infections are common secondary to the immunosuppression inherent to the disease as well as to that induced by chemotherapy. Herpes zoster and unusually large necrotic ulcers of herpes simplex are frequently seen with leukemia (2). Leukemia cutis, in which the skin is infiltrated with leukemic cells, is less common. Its incidence varies according to the type of leukemia. Leukemia cutis occurs in approximately one-third of patients with the monocytic varieties (3) but is rare in acute granulocytic leukemia, with an incidence of less than 5% (2,4,5). Specific lesions usually take the form of papules, nodules, and plaques that are firm, discrete, and pink to purple to reddish brown in color. They vary in size from a few millimeters to solitary lesions of up to 15 cm in diameter (2,6). Macules and ulcers are less frequent (7). The lesions may be hemorrhagic or may blanch on pressure (8). Histologically, infiltrates begin around dermal blood vessels and dermal appendages which remain undisturbed but may be invaded and destroyed later. The epidermis generally remains intact (6). Chloroma, or granulocytic sarcoma, is a green tumor composed of immature granulocytic cells and the only pathognomonic lesion of acute granulocytic leukemia. The green color is due to the presence of myeloperoxidase (1). The lesions of leukemia cutis may progress or regress, either spontaneously or as a result of therapy (6).

Leukemia cutis usually appears after systemic leukemia is diagnosed but may be seen concomitantly or prior to the diagnosis. It has also been described with normal blood and bone marrow findings (9). One report described the occurrence of leukemia cutis after complete remission of acute myelomonocytic leukemia at a time when bone marrow findings revealed no evidence of recurrence (10). These authors supported the hypothesis that the skin may provide a sanctuary for malignant cells during systemic chemotherapy (11).

In acute leukemia, specific cutaneous infiltrates are more often associated with a larger leukemic burden (8,9). One study suggested that leukemia cutis is associated with an adverse prognosis (7).

Case Report

A 64-year-old female presented on November 7, 1988, with extensive cellulitis involving the face, neck, and upper chest wall. Physical examination revealed a temperature of 39°C (102.2°F), mild splenomegaly, and candidal vaginitis. Hemoglobin was 79 g/L (7.9 g/dL), hematocrit 0.23 (23.4%), mean corpuscular volume 97 fl, re-
Fig 1—Skin biopsy showing infiltration of dermis with leukemic cells (hematoxylin-eosin stain, 70X).

ticulocyte count 0.6%, platelet count 115,000/µL, and leukocyte count 6.1 × 10^9/µL with a differential of 57 polymorphonuclear neutrophils, 18 bands, 13 lymphocytes, 6 monocytes, 1 atypical lymphocyte, 2 metamyelocytes, and 3 myelocytes. Antimicrobial therapy included a one-week course of nafcillin. Subsequent peripheral blood smears revealed 10% blast forms with Auer bodies. The leukocyte count never exceeded 10 × 10^9/µL throughout the course of her illness. Bone marrow examination was diagnostic for acute myeloblastic leukemia (French-American-British classification: M2, acute nonlymphoblastic leukemia), with 16% myeloblasts and an overall cellularity of 90%. Almost 85% of the cells stained positive with Sudan black B stain, 76% showed specific granules with alphanaphthol acetate esterase stain, and 14% were positive for butyrate activity (nonspecific esterase). The cellulitis resolved with antibiotic therapy, but a fungating noduloulcerative lesion persisted on the lower lip. Biopsy of this lesion revealed atypical cells which stained positively with chloroacetate esterase stain, indicating an origin from the myeloid series (Fig 1). A course of high-dose cytosine-arabinoside (ara-C) was started on November 23, 1988. The lip nodule improved dramatically and soon disappeared. On November 27th, the patient again developed a high fever, and antibiotic therapy including mezlocillin was instituted. Eight days later, an erythematous macular rash developed over the flanks, lower abdomen, and upper thighs (Fig 2). The rash was nonpruritic and blanched on pressure. The clinical impression was that of a drug reaction secondary to penicillin, and a dermatology consultation concurred with this impression. A punch biopsy was taken to rule out leukemia cutis. The mezlocillin was stopped, and the macules coalesced into large patches which quickly faded, leaving a ruddy brown discoloration. Biopsy revealed leukemic infiltrate (Fig 3). A subsequent bone marrow examination revealed 18%

Fig 2—Leukemia cutis in the form of macular rash.

Fig 3—High power view of biopsy taken from skin rash showing cluster of atypical cells which stained positive with chloroacetate esterase stain.
blasts with an overall cellularity of 5% to 7%. The patient underwent a second course of induction chemotherapy with ara-C combined with mitoxantrone. During this period, adherent whitish plaques developed on the hard palate which sloughed leaving multiple, large, chronic ulcers. Biopsy revealed chronic inflammation without malignant cells. Viral culture was positive for herpes simplex I. A third bone marrow examination showed complete remission.

Discussion

This case illustrates the wide spectrum of specific and non-specific cutaneous lesions that may occur in acute myeloblastic leukemia. Our patient developed two distinct manifestations of leukemia cutis. Neither of these lesions were grossly characteristic of leukemia, and biopsy with cytochemical staining techniques was required for accurate diagnosis. The macular rash was particularly deceptive, masquerading as an allergic drug reaction. Its occurrence after a course of chemotherapy served as a marker, foretelling the presence of incomplete remission. Our observations emphasize the need to biopsy skin lesions of unclear origin in the setting of leukemia.

Our patient also had multiple mucocutaneous infections. Clinicians should suspect an immunosuppressive disorder such as leukemia when confronted with an otherwise unexplained skin infection.

The presence of leukemia cutis may portend an adverse prognosis. Our patient remains in remission on maintenance chemotherapy ten months after initial remission.

References