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CLINICAL REPORT

Aleukemic Leukemia Cutis Presenting as Benign-appearing Exanthema

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Aleukemic leukemia cutis is a rare condition characterized by the infiltration of the skin by leukemic cells before their appearance in the peripheral blood or bone marrow. We report here a 62-year-old seemingly healthy patient who presented with disseminated erythematous maculae. A skin biopsy showed leukemia cutis of monocytic type. No involvement of bone marrow or peripheral blood was found. The patient developed acute monocytic leukemia 7 months later. We present this case to illustrate how leukemia cutis can masquerade as a clinically benign-appearing cutaneous eruption without leukemic changes in blood or bone marrow. To confirm the diagnosis of aleukemic leukemia cutis, immunohistochemistry of the skin lesions as well as a complete staging procedure is necessary. ***Key words: leukemia; skin neoplasms; leukemic infiltration.***

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The leukemias present as malignant neoplasias of white blood cells. They are usually characterized by a diffuse infiltration of the bone marrow and the presence of these neoplastic cells in the bloodstream. In addition, there may be widespread infiltration of internal organs and the skin. We report the case of a patient in whom leukemic changes of the skin preceded involvement of bone marrow and peripheral blood. This rare but well-documented condition is called aleukemic leukemia cutis (1–4).

CASE REPORT

A 62-year-old woman presented with a 6-month history of non-pruritic disseminated skin eruptions. She was otherwise in good health. Physical examination revealed disseminated, erythematous slightly infiltrated maculae with a brown hue located mainly on the trunk, upper arms and legs (Fig. 1). There was no lymph node enlargement, hepatosplenomegaly or gingival hyperplasia. A biopsy specimen showed the entire reticular dermis infiltrated by parallel strands of atypical mononuclear cells with hyperchromatic nucleoli, surrounded by a rim of faintly basophilic cytoplasm (Fig. 2). The tumor cells were found to express the T-cell marker CD43 and the macrophage/monocyte markers CD68 (KP1, PGM-1) and lysozyme (Fig. 3). Only a few cells within the infiltrate were CD3- or CD20-positive lymphocytes. Some leukemic cells were chloracetate esterase- and myeloperoxidase-positive. A diagnosis of leukemia cutis, monocytic type, was made.

The erythrocyte sedimentation rate was 18 mm/h. A complete blood cell count revealed $2.1 \times 10^3/mm^3$ white blood cells with 54% segmented forms and 46% lymphocytes. Red blood cell characteristics, platelets and hemoglobin, as well as a serum chemistry profile and urinalysis, were within normal ranges. Thoracic and abdominal computerized tomography scans showed no abnormalities. Bone marrow aspiration and biopsy from the iliac chest failed to demonstrate leukemic changes. A cytogenetic analysis revealed no chromosomal abnormalities.

A diagnosis of aleukemic leukemia cutis of the monocytic type was made. No treatment was initiated to begin with. Follow-up examinations included a complete blood count every other week and a bone marrow examination every 8–12 weeks. After 7 months, blood counts showed increasing granulocytopenia and anemia and 7% monocytic blasts were found in peripheral blood. Bone marrow examination revealed infiltration of 40% monocytoid blasts. A diagnosis of acute myeloic leukemia, French classification Fab–M5b (acute monocytic leukemia), was made. The patient underwent induction chemotherapy consisting of mitoxantrone, etoposide (VP-16) and cytosine arabinoside (ara C). Complete remission of cutaneous lesions, bone marrow and peripheral blood was achieved. At 4 months follow-up the patient is still receiving chemotherapy and is in complete remission.

DISCUSSION

Two types of skin involvement have been described for leukemia. Non-specific infiltrates occur in up to 40% of patients. They must be distinguished from specific infiltrates known as leukemia cutis (5) in which malignant hematopoietic cells invade the skin. Leukemia cutis is strongly associated with leukemic involvement of bone marrow, peripheral blood and other extramedullary sites. It is most often found in patients with acute monocytic leukemia, in whom it occurs in 25–31% of patients (1, 6). In rare cases, leukemic changes of the skin may precede involvement of peripheral blood and bone marrow. This condition is called aleukemic leukemia cutis (1–4, 7). The diagnosis of aleukemic leukemia cutis may be difficult. Clinically, most patients present with asymptomatic disseminated papulonodules but the clinical manifestations range from a single nodule (8) to erythroderma (9). In the case presented here discrete, erythematous, slightly infiltrated maculae were the only signs of leukemia cutis. Histology and immunohistology, as well as a complete staging procedure, are essential for diagnosis. Typical diagnostic features of leukemia cutis of the monocytic type are testing positive for monocyte/macrophage markers such as CD 68, lysozyme and CD43 or granulocyte markers such as chloracetat esterase and testing negative for pan-T or pan B-cell markers (CD3, CD20) (3, 10). However, one should not rely only on skin biopsy findings in order to determine the type of leukemia (11).

The prognosis of aleukemic leukemia cutis is poor (1, 9, 12–14). Most patients with isolated leukemia cutis will develop bone marrow involvement (15–17). Treatment regimens with chemotherapy alone or in combination with

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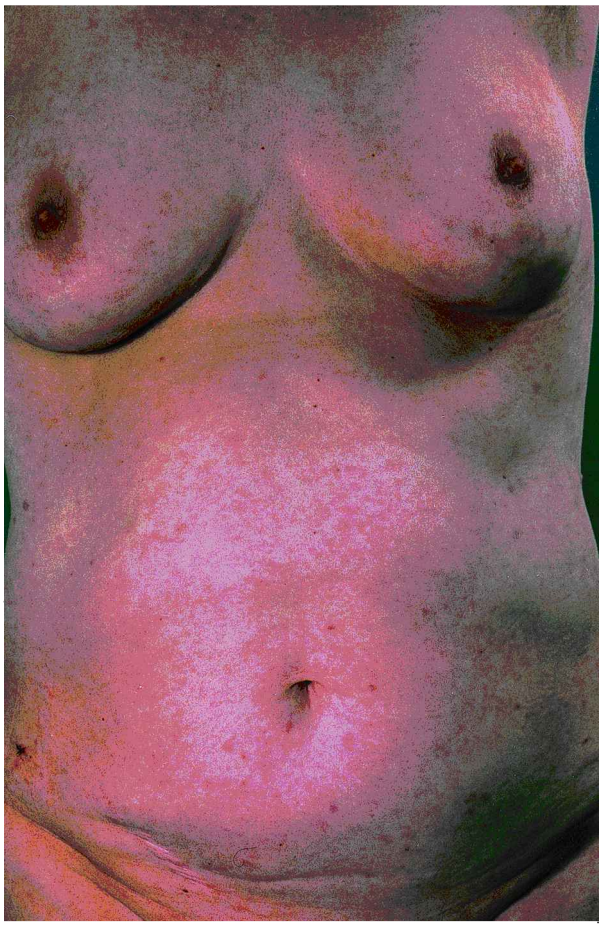

Fig. 1. The patient presented with disseminated, non-pruritic, erythematous, slightly infiltrated maculae.

radiation therapy have been reported. In most cases, treatment was initiated when bone marrow infiltration was found (3, 6, 18). A favorable course of the disease without subsequent development of bone marrow infiltration has been reported for single patients when early treatment with chemotherapy alone or in combination with local therapy was initiated (2, 15, 19, 20). It is unclear if these patients did not develop acute monocytic leukemia due to the aggressive

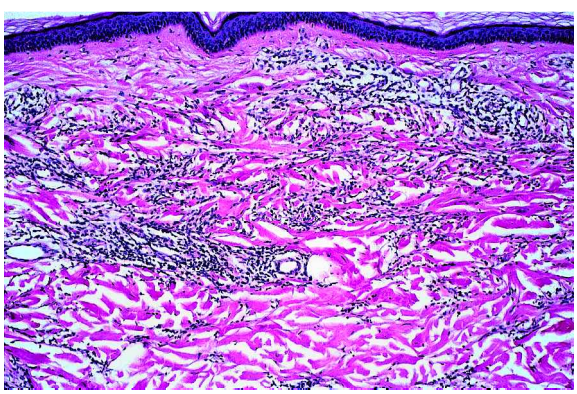

Fig. 2. Diffuse infiltration of the reticular dermis by leukemic cells in horizontal strands between collagen bundles (haematoxylin–eosin staining; original magnification ×13).

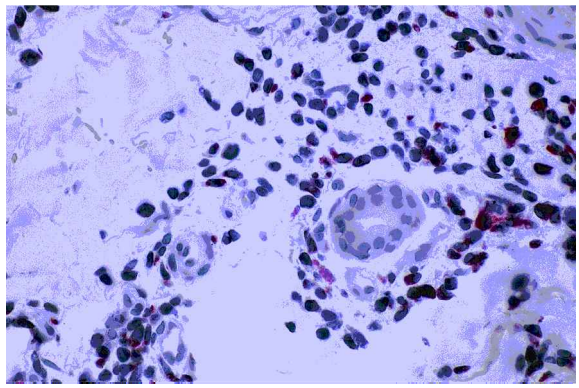

Fig. 3. Immunohistochemistry showing positive labeling for the CD68 antibody KP1 (original magnification ×50).

therapy they received, because their tumor was not inherently aggressive or a combination of both factors. Our patient underwent chemotherapy when acute myeloic leukemia with bone marrow infiltration was diagnosed. She experienced complete remission after induction chemotherapy. However, the follow-up period is too short to draw any definitive conclusions.

We present this case to remind dermatologists that unusual disseminated skin eruptions may be a sign of leukemia cutis even if there are no changes in blood or bone marrow. To confirm the diagnosis of aleukemic leukemia cutis, immunohistochemistry of the skin lesions as well as a complete staging procedure is necessary.

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