Case Report

Aleukemic Monocytic Leukemia Cutis

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Aleukemic leukemia cutis is a rare condition in which leukemic cells invade the skin before they appear in peripheral blood or bone marrow specimens. Herein we describe a 67-year-old man who underwent assessment because of papules and nodules on his back and lower extremities. A biopsy of these lesions confirmed a dense, predominantly monocytic infiltrate of the dermis and subcutaneous tissue. Immunohistochemical stains were positive for CD43 (Leu-22) as well as monocytic markers. Bone marrow and peripheral blood examinations failed to reveal leukemia. Treatment was based on the results of the skin biopsy, and the patient is doing well 1 year after therapy.

REPORT OF CASE

A 67-year-old man underwent assessment in September 1993 at the Mayo Clinic Rochester Department of Dermatology because of papules and nodules on his back (Fig. 1), proximal thigh area, and right forearm. The lesions were asymptomatic, but during the previous year they had grown gradually and were several centimeters in diameter. The patient was otherwise in good health, and the findings on a review of systems were unremarkable. On physical examination, the multiple erythematous papules and nodules varied in size from a few millimeters to several centimeters; the largest was 3.5 by 3 cm. No lymphadenopathy or hepatosplenomegaly was evident.

The results of laboratory tests yielded a normal complete blood cell count and differential and a normal erythrocyte sedimentation rate. Lymphocytoid cytologic studies detected no clonal lymphocyte population. The findings on the following studies were normal: chest roentgenography, electrocardiography, computed tomography of the abdomen and pelvis, Coombs' test, anti-human T-cell lymphotropic virus type I antibodies, chemistry group, protein electrophoresis, and antinuclear antibodies.

A biopsy specimen from the patient’s back showed diffuse infiltration of mononuclear cells into the dermis and subcutaneous fatty tissue (Fig. 2). The cells had abundant cytoplasm and irregularly shaped nuclei, with fine chromatin and prominent nucleoli (Fig. 3). Because these cells seemed to be lymphoid, acute lymphoblastic leukemia or lymphoblastic lymphoma was suspected. Results of the immunohistochemical studies showed that about 15% of the cells stained with 4KB5 (B-cell marker) but were nonreactive for CD20 (L26) or LN2. The T-cell markers showed that 15% of the cells stained with CD45RO (UCHL-1), but virtually all the cells seemed to stain with CD43 (Leu-22). Most of the cells were positive with CD68 (KP1) but were negative for myeloperoxidase and lysozyme.

T- and B-cell molecular genetic studies of the blood and skin biopsy specimens showed no clones. A bone marrow biopsy and a previous examination of the marrow performed elsewhere revealed no abnormality.

Another biopsy specimen was obtained from a nodule on the patient’s back for frozen sections and touch preparations. Massive sheetlike infiltrates of hematopoietic cells were noted in the dermis and subcutaneous tissue. The results of immunohistologic staining of frozen tissue are summarized in Table 1. The final results were interpreted as monocytic leukemia cutis.
The patient underwent a vigorous chemotherapeutic program: daunorubicin, 40 mg/m² by infusion during a 3-day period, in conjunction with cytarabine, 200 mg/m² during a 5-day period. This initial regimen was repeated as soon as the bone marrow recovered. The patient tolerated chemotherapy well and had no complications except for an episode of thrombocytopenia that necessitated platelet transfusion. The cutaneous lesions resolved quickly, and the patient has remained free of the disease for 1 year.

DISCUSSION

Cutaneous manifestations of leukemia can be divided into two groups: nonspecific leukemic lesions that contain no leukemic cells and occur in about 30% of patients with leukemia and the less common leukemia cutis lesions that represent a true leukemic cell infiltrate into the skin. Monocytic leukemias are more likely to involve the skin than are granulocytic or lymphocytic leukemia.

Aleukemic monocytic leukemia cutis is a rare condition characterized by leukemic cells that invade the skin before they appear in peripheral blood or bone marrow specimens. Whether the leukemic clone originates in the bone marrow with early seeding to extramedullary sites or whether its origin is extramedullary with hematogenous spread to bone marrow and other sites is unknown. Histologically, a diffuse infiltration of mononuclear cells into the dermis and subcutaneous fatty tissue is evident. The cells have abundant cytoplasm and irregularly shaped nuclei, with fine chromatin and prominent nucleoli.

Immunohistochemical markers are important in the diagnosis of hematopoietic infiltrates. A CD3, CD20 (L26), and CD43 (Leu-22) panel is used routinely for formalin-fixed, paraffin-embedded tissues. In the current case, CD43 (Leu-22) was the only marker that stained most of the tumor cells. A lack of specificity of CD43 is a characteristic that must be recognized when this antibody is incorporated into a diagnostic immunophenotyping panel. In the review by Segal and associates of 17 cases of "CD43 only" phenotype in patients who lacked the expression of CD20 (L26) and CD45RO (UCHL-1), 8 cases were extramedullary leukemic infiltrate (5 myeloid, 2 monocytic, and 1 mixed lineage), 4 were T-cell lymphoma, 3 were B-cell lymphoma, and 2 were plasmacytomas.

In the current case, the lack of expression of B-cell markers (4KB5, CD19, CD20, LN2, and κ and λ light chains), T-cell markers (CD3, CD4, CD5, and CD7), and negative T- and B-cell gene rearrangement of blood and skin tissue specimens excluded the possibility of a B-cell or T-cell...
Table I.—Results of Immunoperoxidase Studies of Paraffin and Frozen Sections of Skin Biopsy Specimens*

<table>
<thead>
<tr>
<th>Paraffin-embedded sections</th>
<th>Frozen tissue sections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Result</td>
</tr>
<tr>
<td>CD45RO (UCHL-1)</td>
<td>+</td>
</tr>
<tr>
<td>CD43 (Leu-22)</td>
<td>+++</td>
</tr>
<tr>
<td>CD68 (KP1)</td>
<td>+++</td>
</tr>
<tr>
<td>Myeloperoxidase</td>
<td>–</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>–</td>
</tr>
<tr>
<td>4KB5</td>
<td>+/-</td>
</tr>
<tr>
<td>CD20 (L26)</td>
<td>–</td>
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<tr>
<td>LN2</td>
<td>–</td>
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</table>

*+++ = >75% of malignant cells; ++ = 50-74% of malignant cells; + = 25-49% of malignant cells; and +/- = <25% of malignant cells.

lymphoma. The negative myeloperoxidase and lysozyme eliminated the possibility of myelocytic leukemia or granulocytic sarcoma. Most of the tumor cells were positive with CD68 (KP1), CD13, and CD14, a situation that suggested a monocytic differentiation. The absence of bone marrow involvement on three occasions established the diagnosis of aleukemic monocytic leukemia cutis.

In a study by Su and colleagues11 of 42 patients with leukemia cutis, 7% had specific skin lesions that preceded involvement of the peripheral blood. Burg and coworkers1 and other investigators35,6 described a total of seven patients who had extramedullary disease that resembled lymphoma (clinically and histologically). Acute monocytic leukemia was diagnosed subsequently on the basis of morphologic and cytochemical studies of peripheral blood and bone marrow samples. Two other cases of acute myelomonocytic leukemia that resembled lymphoma cutis have been reported.5,4 Because both granulocytic and monocytic cells originate from a common stem cell, cases of acute monocytic leukemia occasionally show granulocytic cells or even transform from a pure monocytic to a myelomonocytic leukemia.3

CONCLUSION
In the current case of aleukemic monocytic leukemia cutis, the CD43 only phenotype on routine immunoperoxidase studies done with paraffin-embedded tissues was a clue for the diagnosis and led to immunoperoxidase studies of frozen tissue sections, which were necessary for the final diagnosis. This case is extremely unusual in that the diagnosis was made and treatment was initiated solely on the basis of a positive skin biopsy result. The patient received chemotherapy and currently is free of disease after 1 year, despite the expected poor prognosis.

REFERENCES
5. Miliauskas JR. Dermal monocytic sarcoma/monoblastic tumour: report of two cases of acute monocytic leukemia with initial dermal manifestations only. Pathology 1986; 18:249–253