Leukemia Cutis Masquerading as Vitiligo

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Chronic myelomonocytic leukemia (CMML) is a hematologic stem cell disorder with myelodysplastic and myeloproliferative characteristics. Extramedullary leukemic infiltration of the skin, although uncommon in CMML, has prognostic relevance. We report a unique case of a patient with CMML who clinically presented with vitiligo that was histologically diagnosed as leukemia cutis. This case underscores the necessity of early recognition of skin changes in patients with hematologic disorders and the differentiation of nonspecific skin lesions from leukemia cutis.

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Chronic myelomonocytic leukemia (CMML) is a clonal disorder of hematopoietic stem cells with features of myelodysplastic syndrome (MDS) characterized by monocytosis and refractory anemia with excess blasts, as well as myeloproliferative syndrome with leukocytosis, neutrophilia, monocytosis, and splenomegaly. CMML most frequently presents in patients older than 60 years and often proves refractory to chemotherapy. The onset of specific cutaneous manifestations such as pyoderma gangrenosum, Sweet syndrome, and leukemia cutis in MDS are associated with an aggressive course and poor long-term survival.[1,2] While skin infiltration of leukemic cells is well-documented in acute myelogenous leukemia (AML), leukemia cutis in CMML is less frequent. We describe a case of leukemia cutis that clinically appeared as vitiligo, an autoimmune disease in which T lymphocytes mediate the destruction of melanocytes.

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Case Report

A 57-year-old man presented with hypopigmented macules over his left forearm that had gradually appeared over 2 months. The patient's CMML was diagnosed 4 months prior to his presentation to us. There was no personal or family history of autoimmune disease. At the time of CMML diagnosis, the peripheral blood showed a marked monocytosis of 1.3×10^9 cells/L (reference range, $0.2–0.8\times10^9$ cells/L) and abnormal granulocytic maturation. Bone marrow aspirate demonstrated decalcified hypercellular marrow, maturing trilineage hematopoiesis, and dysplastic megakaryocytes. Immunophenotyping by flow cytometry confirmed the presence of a large monocytic cluster expressing abnormal CD56 and monocytic antigens CD14, CD64, CD33, and CD4. Fluorescent in situ hybridization and polymerase chain reaction were both negative for the breakpoint cluster region–Abelson gene, *BCR-ABL*. Cytogenetic analysis revealed trisomy 8, loss of Y, and rearrangement of the short arm of 1.

Physical examination showed hypopigmented macules, several of which coalesced into patches on the left forearm (Figure 1). The remainder of the examination was unremarkable. The hypopigmented macules were clinically thought to be vitiligo, tinea versicolor, leukemic infiltrate, or mycosis fungoides. Histopathology from a core biopsy revealed a superficial and mid-dermal perivascular mononuclear infiltrate of mild density (Figure 2). The cells demonstrated hyperchromatism, nuclear enlargement, and a small rim of cytoplasm (Figure 3).

The patient underwent 4 cycles of chemotherapy with azacitadine but developed acute myelomonocytic leukemia and succumbed to a blast crisis. He died 10 months after the original CMML diagnosis.

Comment

While cutaneous manifestations in leukemia are commonly due to inflammatory conditions, infections, and graft versus host disease, leukemia cutis is rare. Extramedullary leukemic skin infiltrate often heralds an aggressive course and the transition to refractory anemia with excess blasts.[3]

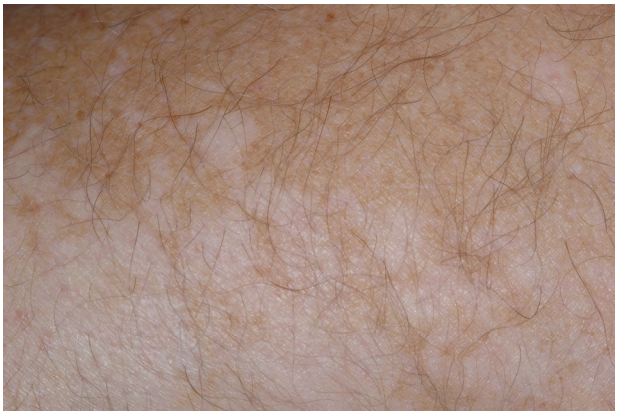

Figure 1. Hypopigmented macules coalesced into patches on the left forearm.

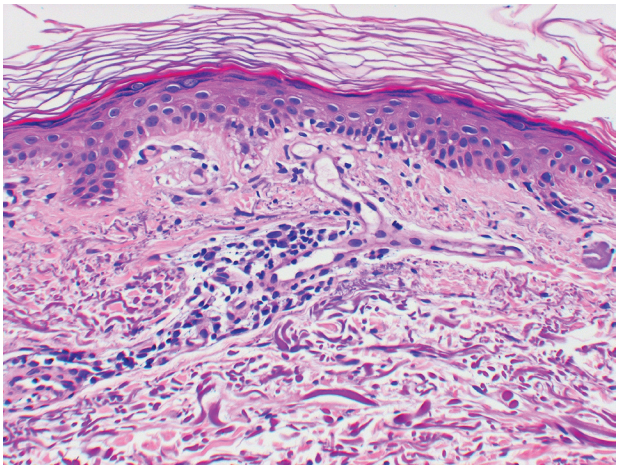

Figure 2. Superficial and mid-dermal perivascular mononuclear infiltrate (H&E, original magnification ×100).

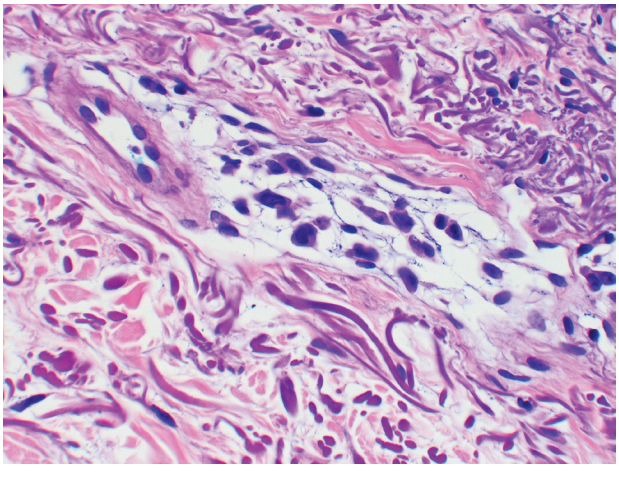

Figure 3. Mononuclear infiltrating cells demonstrated hyperchromatism, nuclear enlargement, and a small rim of cytoplasm (H&E, original magnification ×400).

Skin infiltration may correlate with the onset of systemic disease, indicate disease recurrence, be confined to the skin (aleukemic leukemia cutis), or present as the initial sign of leukemia. The incidence of leukemia cutis is most frequently associated with AML, particularly the monocytic (M5) and myelomonocytic (M4) subtypes of leukemia from the French-American-British classification system.[4]

Cutaneous involvement is well-established in AML; however, it is the exception in CMML. Of the reported cases of cutaneous manifestations in CMML, the lesions presented as pruritic, erythematous, maculopapular eruptions; skin nodules; infiltrated plaques; and bullous lesions, occurring on the chest wall, face, thighs, and genitals.[5,6] Uniquely, our case of leukemia cutis presented as vitiligo, which, to date, has not been reported in CMML. Vitiligo has been associated with Sézary syndrome and cutaneous T-cell lymphoma (CTCL). Alcalay et al[7] reported the first case of Sézary syndrome and vitiligo confirmed by a biopsy specimen demonstrating a dense dermal lymphocytic infiltrate composed of helper T cells, which suggested that the epidermal destruction of melanocytes could be induced by cell-mediated immunity associated with cytotoxic T cells. Furthermore, it has been proposed that a subpopulation of T cells may recognize specific melanocytic epitopes, thus inducing hypopigmentation changes. In one patient, Knol et al[8] found a correlation between vitiligo and cutaneous T-cell lymphoma with the presence of a T-lymphocyte subpopulation reactive against the melanocyte differentiation antigen Melan-A/MART1 detected in skin lesions.

The variable presentation of leukemia cutis and the high occurrence of nonspecific skin lesions in patients with leukemia require histologic differentiation of leukemia cutis from nonspecific cutaneous conditions that occur more frequently in patients with leukemia.[2,3] Observation of myeloblasts and positivity of the myeloid sensitive marker, lysozyme, support a diagnosis of leukemia. Moreover, certain genetic aberrancies have been linked with the development of leukemia cutis and central nervous system complications, including trisomy of chromosome 8, which our patient demonstrated, as well as t(8;21)(q22;q22).[9,10]

Most patients with leukemia cutis die of acute leukemia within 5 months of the onset of skin manifestations despite chemotherapy and total body electron beam radiation.[2] A high suspicion

of leukemia cutis is required in patients with MDS presenting with cutaneous manifestations because leukemia cutis can imitate a variety of inflammatory, fungal, and, as in our case, autoimmune diseases.

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