

A 68 YEAR-OLD WOMAN WITH LEUKEMIA UNDER HER SKIN

Ben Creelan, MD, Hari Nair, MSIII, and Joanne Filicko-O'Hara, MD

Introduction

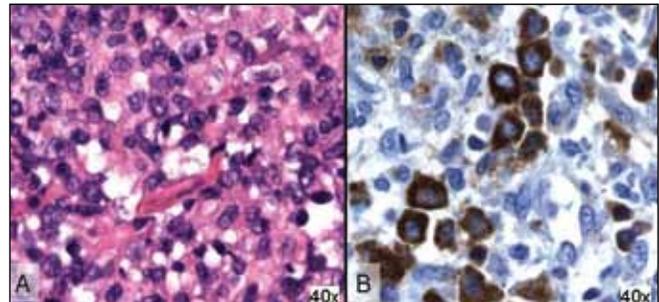
A wide spectrum of skin manifestations occurs in leukemia. Skin lesions are often due to infection, drug reaction, or inflammation.¹ Rarely, extramedullary leukemia can invade the skin and is called leukemia cutis.² Leukemia cutis is the infiltration of neoplastic leukocytes into the dermis or subcutaneous tissue, resulting in an identifiable skin lesion. These lesions show a varied morphology, and confirmatory immunohistochemical stains are needed for the diagnosis. Leukemia cutis may occur before, after, or concomitantly with the onset of systemic leukemia.³ Here we report a case of leukemia cutis occurring simultaneously with newly diagnosed acute myelogenous leukemia.

Case Report

A 68 year-old Caucasian female presented with a dry cough and malaise for two weeks. She noted fever as high as 101°F for the past two days. The patient reported visiting her primary care physician the previous week for routine lab work. She was contacted by her primary doctor and told to go to the ER because of decreased platelets and increased white blood cells. The patient did not take any medications. Past medical history was significant for spinal surgery in 1996 and 2001, which was

complicated by superficial bacterial infection. She had never smoked, used alcohol or illicit substances. Allergy and family history was noncontributory.

Figure 2. Dermal biopsy of the skin lesion demonstrates infiltrating atypical cells (image A) expressing myeloperoxidase and focally CD38 (image B).



Physical exam was significant for a papule on the right cheek. This erythematous, firm papule had well-defined borders measuring approximately 3 x 2 cm above the nasolabial fold on the right cheek (Figure 1). The patient attributed this to mosquito bites during a recent weekend camping trip. Laboratory testing revealed leukocytosis (30 x 10⁹/l), anemia (7.3 g/dL) and



Figure 1. An erythematous firm papule is located on right facial cheek of the patient.

thrombocytopenia (50 x 10⁹/l). Manual differentiation revealed 31% blast cells. Bone marrow biopsy revealed acute myelogenous leukemia with multilineage dysplasia (AML, FAB M4). A single punch skin biopsy to a depth of 40 millimeters was performed. The biopsy showed dermal infiltrates of atypical cells expressing myeloperoxidase and focally CD38 (Figure 2). A c-kit stain revealed infiltration of mast cells consistent with leukemia cutis. The patient was treated with induction cytarabine and idarubicin, and her leukemia cutis lesion resolved within one week of initiation of chemotherapy. Her day #14 and day #30 bone marrow biopsies revealed no residual neoplastic disease.

Discussion

Patients with AML generally present with vague complaints related to complications of pancytopenia including weakness and easy fatigue.⁴ Skin findings in AML commonly include pallor, petechiae, or ecchymoses. Leukemic involvement of the skin is uncommon. When present, it is most often found in patients with monocytic or myelomonocytic AML variants.⁵ The overall incidence of leukemia cutis in AML is unclear but varies from 3% to 13% in separate case series.⁶ About 23% to 44% of leukemia cutis is diagnosed at the same time as the systemic malignancy, as in our case. Less than 10% are discovered before systemic disease can be identified, and the remainder of cases appears afterwards.⁷ The frequency of leukemia cutis is much higher in children with congenital leukemia; in fact as many as 25% to 30% of infants develop cutaneous involvement. In contrast to adult disease, this does not confer a worse prognosis.⁸

Leukemia cutis is due to the local proliferation of leukemic cells into the dermis, epidermis, and subcutaneous tissue. The underlying molecular basis for the migration of leukemic cells to the skin is still unclear. It is hypothesized that the two ligands, Thymus Activation-Regulated Chemokine (TARC/CCL17) and Macrophage-Derived Chemokine (MDC/CCL22) are expressed on the skin, which attract adult T-cell leukemic cells to the skin. T-cell related antigens are also present on the cell surface of leukemic cells in acute monocytic leukemia (AML-M5), which may promote selective tropism of these cells to the skin surface.⁹ Additional studies have shown Cutaneous Lymphocyte-associated Antigen (CLA) staining in 78% of patients with myelomonocytic leukemia cutis patients, suggesting that CLA may play a role in leukemic invasion of the skin.¹⁰

The classic lesions of leukemia cutis are red-brown to violaceous-plum papules or plaques of varying sizes.¹¹ The legs are involved most commonly, followed by arms, back, chest, scalp and face. Due to the varied clinical presentation, a biopsy of the lesion with immunohistochemical studies is often necessary. Histological findings of leukemia cutis typically show a diffuse

infiltration of leukemic cells in the dermis and subcutaneous tissue, often squeezed between collagen bundles. Involvement of blood vessels and skin adnexa are seen in the granulocytic, monocytic and myelomonocytic variants of leukemia cutis.¹²

The development of leukemia cutis portends a poor prognosis in adults. More than 90% of these patients will have other sites of extramedullary involvement, and in 40% of these cases, the meninges will be involved.^{13,14} The disease course is usually aggressive, and length of survival is short. Studies have shown that the average survival time in AML patients with leukemia cutis is 7.5 months, and the overall survival rate is 6% at 2 years compared to 30% in AML patients without leukemia cutis¹⁵. Even with this poor prognosis, long-term disease-free survival is possible with curative therapy directed at the skin, bone marrow and other sites of extramedullary involvement.¹⁶

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