

## BRIEF ARTICLE

**Leukemia Cutis as the Presenting Sign of Acute Myeloid Leukemia in an HIV+ patient**

Natalie Garcia, BS<sup>1</sup>, Charlotte Mcrae, BS<sup>1</sup>, Abigail Smith, MD<sup>2</sup>, Lauren Graham, MD, PhD<sup>2</sup>

<sup>1</sup>University of Alabama at Birmingham Heersink School of Medicine, Birmingham, AL

<sup>2</sup>University of Alabama at Birmingham, Department of Dermatology, Birmingham, AL

**ABSTRACT**

Leukemia Cutis (LC) is a rare extramedullary cutaneous manifestation of leukemia that varies in terms of clinical presentation, leukemia type, and timing of presentation in relation to systemic leukemia. LC typically presents following diagnosis of systemic leukemia and during an active flare or relapse. An estimated 3.7% of patients with Acute Myeloid Leukemia (AML) develop LC. A 61-year-old male with poorly controlled HIV presented with a rash that began one month prior on his cheek as a red papule, which he believed was an ingrown hair. On exam, pink and yellow firm papules and nodules covered his entire body surface except the groin and axilla. One nodule held a peau d'orange appearance. The rash was overall asymptomatic, and he reported only increased fatigue. His CD4 count and viral load were 136 and 330,000 respectively. One punch biopsy revealed negative cultures for fungus, bacteria, and acid-fast bacilli. Two biopsies sent for pathologic evaluation revealed AML of the skin. Bone marrow biopsy confirmed AML. Clinically the presentation of LC is nonspecific, and systemic symptoms rarely appear in conjunction with LC. High clinical suspicion and histopathologic examination are necessary for diagnosis of LC.

**INTRODUCTION**

Leukemia Cutis (LC) is a rare extramedullary cutaneous manifestation of leukemia that varies in terms of clinical presentation, type of leukemia, and timing of presentation in relation to systemic leukemia. Rapidly developing bone marrow insufficiency causes leukemia and subsequent metastatic disease, which results in a wide array of cutaneous manifestations. LC presents with nonspecific skin findings which may mimic lesions found in other inflammatory, benign, or malignant conditions. LC typically presents during an active flare of leukemia or during relapse, but it rarely presents as the primary

manifestation of systemic leukemia. A high index of suspicion is often necessary for diagnosis and driven by the clinician's review of systems, physical exam, and evaluation of other co-morbid conditions.

Immunosuppressed patients, due to immunosuppressive medications taken to treat systemic auto-inflammatory diseases or conditions such as HIV/AIDs, are at higher risk for the development of secondary malignancies, particularly leukemia and lymphoma. HIV infection decreases the CD4 count and causes dysregulation of CD4 and CD8 activation. CD4 and CD8 cells play an important role in both cancer surveillance and the inactivation of oncogenic viruses. Thus,

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even patients with adequate viral load suppression and a normal CD4 count also have an increased risk of malignancy.<sup>1</sup> We present the case of an HIV positive male who developed diffuse dermal nodules, with subsequent biopsy revealing cutaneous leukemic metastases.

## CASE REPORT

A 61-year-old male with a past medical history of poorly controlled HIV presented to dermatology clinic with a new rash. The rash initially started one month prior to presentation on the patient's cheek as a single red papule, which the patient believed to be an ingrown hair. The rash then spread to cover all surfaces of his body except his groin and axilla. On exam, pink and yellow firm papules and nodules covered nearly his entire body surface (**Figure 1 and 2**). The first nodule to appear on the patient's trunk was on the left shoulder and held a peau d'orange appearance. The patient reported that the rash was overall asymptomatic, as he was not in pain, did not itch, and had not experienced drainage or oozing from any of the nodules. The patient also denied systemic symptoms of chills, fever, weight



**Figure 2.** Leukemia cutis. There are numerous pink to salmon-colored firm papules and nodules on the trunk.

loss, night sweats, and swollen lymph nodes; however, he experienced fatigue following the onset of the rash.



**Figure 1.** Leukemia Cutis. (**Left**) The nodules over the extremities have a more violaceous appearance. (**Right**) The first nodule to appear on the patient's trunk was on the posterior left shoulder and held a peau d'orange appearance.

At the time of presentation, the patient's last charted CD4 count and viral load were 136 and 330,000 respectively. Review of clinic notes suggested the patient had been instructed to discontinue his anti-retroviral therapy (ART) pending evaluation of his rash. Due to subsequent lack of improvement of his rash, he was restarted on ART. The differential diagnosis based on clinical history and presentation included reticulohistiocytosis, mastocytosis, erythema elevatum diutinum, other granulomatous disorders, B-cell lymphoma, and atypical infectious etiologies given his low CD4 count. One punch biopsy sent for tissue culture was negative for fungus, bacteria, and acid-fast bacilli. Two punch biopsies sent for pathologic evaluation revealed acute myeloid leukemia (AML) of the skin, resulting in the diagnosis of leukemia cutis (LC).

Subsequent bone marrow aspirate was obtained, and gross examination revealed hypercellular marrow with no overt dysplasia or increase in blasts. Cytogenetic testing revealed an abnormal AML fluorescence in

situ hybridization (FISH) panel, which demonstrated that 3.6% of the cells had a rearrangement involving the KMT2A gene at 11q23.

## DISCUSSION

Clinically the appearance of LC is nonspecific, ranging from solitary to multiple papules, nodules, blistering ulcers, or diffuse rash classically of the extremities.<sup>2</sup> Abnormal cutaneous findings in this patient led to cytogenetic bone marrow aspirate analysis, which revealed a rearrangement in the KMT2A gene responsible for the regulation of hematopoiesis and gene expression.<sup>3</sup> This patient was ultimately diagnosed with acute myeloid leukemia (AML), and only 2.9-3.7% of patients with AML are estimated to develop LC.<sup>2</sup> Of the patients with AML who develop LC, only 7% of those patients present without systemic evidence of leukemia. Thus approximately 0.2% of patients with AML will present with LC in the absence of abnormal complete blood count, bone marrow aspirate, or peripheral blood smear.<sup>2</sup> Classic symptoms of leukemia, such as thrombocytopenia, anemia, and fever, rarely appear in conjunction with LC, as was the case with our patient.<sup>4</sup>

## CONCLUSION

The presentation of LC does not follow a clear pattern, and clinical observation alone cannot ensure definitive diagnosis. A thorough history, high clinical suspicion, histopathologic examination, blood work, and bone marrow analysis are important for the diagnosis of LC due to its range of presentations, classifications, and timing. The diagnosis of leukemia cutis is important to consider, regardless of CD4

count or presence of systemic leukemia, in immunosuppressed patients.

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**Corresponding Author:**

Natalie Garcia, BS  
University of Alabama at Birmingham  
Heersink School of Medicine  
Email: nhvoss@uab.edu

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