

Rare case of leukemia cutis presenting as erythroderma in a patient with acute myeloid leukemia



Marie Donaldson, BA,^a Matthew I. Ebia, MS,^a Joshua L. Owen, MD, PhD,^a and Jennifer N. Choi, MD^{a,b}
Chicago, Illinois

Key words: acute myeloid leukemia; cutaneous leukemia; erythroderma; exfoliative dermatitis; leukemia cutis.

INTRODUCTION

Leukemia is a malignancy of the hematopoietic system clinically characterized by nonspecific systemic symptoms; however, many leukemia subtypes exhibit cutaneous manifestations.¹ These findings may be classified as either unspecific, indicating associated nonleukemic dermatologic disease, or specific, denoting infiltration of leukemic cells into the epidermis, dermis, or subcutaneous tissue. These specific findings are known as leukemia cutis (LC), and may precede, follow, or occur concomitantly with systemic leukemia.² LC may present as single or multiple lesions, most commonly on the trunk and extremities, but may also be disseminated.³ LC can present as a variety of morphologies³ but is most commonly described as pink, red-brown, or violaceous papules, nodules, and plaques.

Erythroderma is an inflammatory reaction characterized by erythema, pruritus, and scaling of the skin, typically presenting diffusely and covering most or all of the body, commonly defined as greater than 90% body surface area (BSA),⁴ although some references define it as at least 70% BSA.⁵ The most common causes include progression of existing dermatoses, drug reactions, underlying malignancy, or idiopathic causes.⁴ We present a case of a patient with newly diagnosed acute myelogenous leukemia (AML) who had erythrodermic LC shortly after induction chemotherapy.

CASE REPORT

A 50-year-old woman with no significant medical history had flu-like symptoms, including body aches, nausea, and sore throat, and was found to have a

Abbreviations used:

AML: acute myelogenous leukemia
BSA: body surface area
LC: leukemia cutis

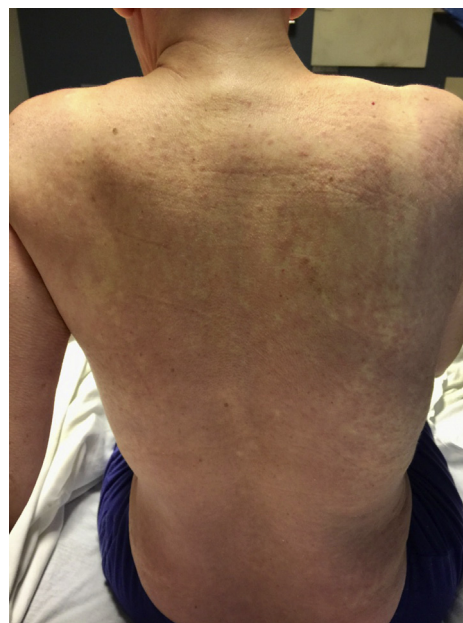


Fig 1. Clinical presentation. On the scalp, back, abdomen, and chest, there were numerous 3- to 5-mm pink papules coalescent into confluent plaques on the abdomen and back.

white blood cell count of 200,600/ μ L. Further clinical workup, including bone marrow biopsy, cytogenetic analysis, and flow cytometry, led to the diagnosis of

From the Department of Dermatology, Northwestern University Feinberg School of Medicine^a and Robert H. Lurie Comprehensive Cancer Center of Northwestern University.^b

Funding sources: None.

Conflicts of interest: None disclosed.

Correspondence to: Jennifer N. Choi, MD, 676 N Saint Clair, Suite 1600, Chicago, IL 60611. E-mail: Jennifer.choi@northwestern.edu.

JAAD Case Reports 2019;5:121-3.

2352-5126

© 2018 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2018.10.019>

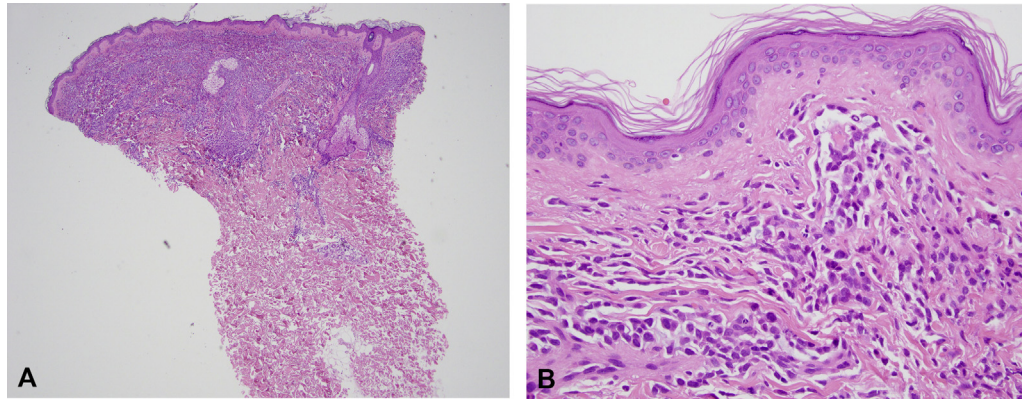


Fig 2. Histopathology of LC. **A**, Punch biopsy shows a monomorphous infiltrate that fills the papillary dermis beneath a Grenz zone. **B**, Higher magnification shows intermediate size mononuclear cells with abundant cytoplasm and oval nuclei that are intercalating between the collagen bundles; a Grenz zone is again noted. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, $\times 40$; **B**, $\times 400$.)

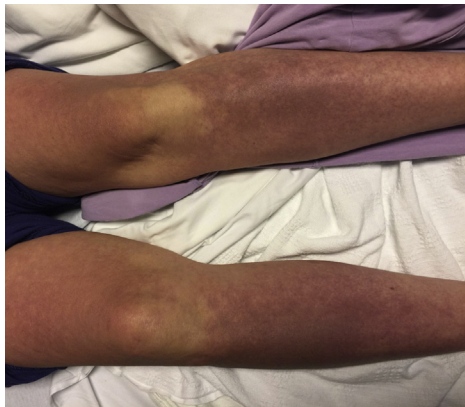


Fig 3. Confluent deeply erythematous to violaceous patches covered the bilateral arms and legs. Overall, these patches and plaques covered 70% BSA, consistent with erythroderma.

FLT3 D835 mutation-positive AML. Immediately after diagnosis, she underwent induction treatment with 7 days of cytarabine and 3 days of daunorubicin. After completion of induction therapy, a bone marrow biopsy was negative for residual disease.

Three days after completing chemotherapy, she presented to the dermatology department with a diffuse erythematous and violaceous eruption across the arms, chest, trunk, and legs, consistent with erythroderma (Fig 1). Punch biopsy of the lesion found a monomorphous infiltrate beneath a Grenz zone composed of intermediate size mononuclear cells with abundant cytoplasm and oval nuclei, consistent with LC (Fig 2). Given these findings, she was admitted for reinduction treatment, and the dermatology department was consulted for re-

evaluation of her skin findings given her atypical clinical presentation for LC.

Physical examination found numerous erythematous to violaceous papules on the scalp, chest, abdomen, and upper back, which coalesced into confluent plaques and patches on the back and abdomen (Fig 1). Morbilliform violaceous, confluent, blanchable patches were seen on her bilateral upper and lower extremities (Fig 3). Overall, the eruption involved approximately 70% of her body surface area. There was no mucocutaneous involvement. Repeat punch biopsy of a papule on the right breast found a similar inflammatory reaction pattern to that of the previous biopsy with immunohistochemistry showing tumor cells positive for lysozyme and CD68 and negative for myeloperoxidase, CD56, and TCL1 (Fig 2, A and B). This finding was consistent with a diagnosis of LC associated with AML with monocytic differentiation. Reinduction therapy with high-dose cytarabine for 7 days led to complete resolution of the eruption within 2 weeks, and a repeat bone marrow biopsy was negative for residual disease.

Three months after initial diagnosis, she underwent an allogeneic unrelated donor hematopoietic stem cell transplant. She has not had any recurrence of cutaneous or systemic leukemia for the last 2 years and continues to be in remission.

DISCUSSION

Of leukemia subtypes, AML is the most likely to develop LC,¹ and the prevalence of biopsy-proven LC in patients with this subtype has been reported as 2.9%.⁶ Patients with different leukemia subtypes may have a wide variety of cutaneous

Table I. Erythrodermic LC reported in the literature

Study	Patient age (y), sex	Leukemia subtype	Treatment	Erythroderma at presentation	BSA involved	Patient outcome
Su et al, 1984 ^{9*}	NR	Chronic lymphocytic leukemia	NR	Yes	NR	NR
Jeong et al, 2009 ⁷	82, male	Small cell variant of T-cell prolymphocytic leukemia	Oral fludarabine and prednisone	Yes	100% [†]	Death within 2 wks of chemotherapy initiation
Raj et al, 2011 ⁸	75, male	Chronic myeloid leukemia	Imatinib	Yes	NR	Resolution within 1 mo of imatinib treatment
Novoa et al, 2015 ⁵	65, female	Pre-B-cell acute lymphoblastic leukemia	Hospice care	No	70%	Death
Current case, 2018	50, female	AML	Cytarabine, HSCT	No	70%	Resolution within 2 wks of cytarabine reinduction

HSCT, Hematopoietic stem cell transplant; NR, not reported.

*Su et al describe 2 cases of erythroderma in patients with CLL as a part of a case series. It is not explicitly described whether the erythroderma was caused by leukemic infiltration of the skin or if it was related to the underlying leukemia.

[†]Jeong et al describe involvement of the whole body although do not explicitly quantify the BSA involvement.

manifestations, but only 4 other cases have been reported in the literature of LC presenting as erythroderma (Table I).^{5,7-9} Of the cases reported, there is an equal ratio of male to female patients, and both acute and chronic subtypes of leukemia are represented. The prognosis for these patients ranges from death to full resolution of the leukemia after treatment.

Prognosis remains poor in patients with LC. Treatment is aimed at addressing the underlying leukemia, which is dictated by subtype and the patient's tolerance of systemic therapy. Radiation therapy, specifically total skin electron beam therapy, is found to be an effective treatment for cutaneous disease, but systemic chemotherapy remains the treatment modality of choice.¹⁰

To our knowledge, this is the first reported case of a patient with AML subsequently having erythrodermic LC. Erythroderma represents a rare, but important presentation of LC that should be included in the differential diagnosis of erythroderma. LC may manifest as a variety of morphologies, and a high level of suspicion may be necessary to facilitate early recognition. Accurate diagnosis with skin biopsies to provide histopathologic and immunohistochemical information is crucial for subsequent treatment, prognosis, and overall patient quality of life.

REFERENCES

1. Wagner G, Fenchel K, Back W, Schulz A, Sachse MM. Leukemia cutis - epidemiology, clinical presentation, and differential diagnoses. *J German Soc Dermatol.* 2011;10:27-36.
2. Wagner LI, Berg SR, Gandhi M, et al. The development of a Functional Assessment of Cancer Therapy (FACT) questionnaire to assess dermatologic symptoms associated with epidermal growth factor receptor inhibitors (FACT-EGFR-18). *Support Care Cancer.* 2013;21:1033-1041.
3. Kang YS, Kim HS, Park HJ, et al. Clinical characteristics of 75 patients with leukemia cutis. *J Korean Med Sci.* 2013;28:614-619.
4. Tan GF, Kong YL, Tan AS, Tey HL. Causes and features of erythroderma. *Ann Acad Med.* 2014;43:391-394.
5. Novoa RA, Wanat KA, Rosenbach M, Frey N, Frank DM, Elenitsas R. Erythrodermic leukemia cutis in a patient with pre-B-cell acute lymphoblastic leukemia. *Am J Dermatopathol.* 2015;37:650-652.
6. Agis H, Weltermann A, Fonatsch C, et al. A comparative study on demographic, hematological, and cytogenetic findings and prognosis in acute myeloid leukemia with and without leukemia cutis. *Ann Hematol.* 2002;81:90-95.
7. Jeong KH, Lew BL, Sim WY. Generalized leukaemia cutis from a small cell variant of T-cell prolymphocytic leukaemia presenting with exfoliative dermatitis. *Acta Dermato-venereologica.* 2009;89:509-512.
8. Raj A, Rai R, Rangarajan B. Exfoliative dermatitis with leukemia cutis in a patient with chronic myeloid leukemia: A rare association. *Indian J Dermatol Venereol Leprol.* 2011;77:208-210.
9. Su WP, Buechner S, Li CY. Clinicopathologic correlations on leukemia cutis. *J Am Acad Dermatol.* 1984;11:121-128.
10. Elsayad K, Oertel M, Haverkamp U, Eich HT. The effectiveness of radiotherapy for leukemia cutis. *J Cancer Res Clin Oncol.* 2017;143:851-859.