CASE REPORT
Year: 2020 • Volume: 3 • Issue: 2 • Page: 48-50

LEUKEMIA CUTIS IN ACUTE PROMYELOCYTIC LEUKEMIA: A RARE ENTITY

Subhashini Konala[1], Satya Saka[1], Priyadarshini Dantuluri[1], Seetharamanjaneyulu Kolalapudi[1]
[1]Department of Dermatology ,Venereology and Leprosy, GSL Medical College and General Hospital, Rajahmundry , Andhra Pradesh
Corresponding Author:
Dr Satya Saka
Asso. Professor,
Department of Dermatology,Venereology and Leprosy, GSL Medical College and General Hospital,
Rajahmundry, Andhra Pradesh • Email: satyaikon@gmail.com

Abstract

Leukemia cutis is cutaneous infiltration by neoplastic leukocytes (myeloid or lymphoid) and indicates grave prognosis. It occurs mostly in acute myelomonocytic (AML-M4) and monocytic (AML-M5) subtypes of acute myeloid leukemia. In acute promyelocytic subtype (AML-M3), the skin lesions are rare but may occur after treatment with all-trans retinoic acid (ATRA).We report a case of leukemia cutis presented with plaques with haemorrhagic vesicles in acute promyelocytic (AML-M3) subtype before starting ATRA, which is very rare.

Key words: leukemia cutis, leukemia, promyelocytic, auer rods, all-trans retinoic acid.

Introduction

Leukemia cutis (LC) is defined as cutaneous infiltration by neoplastic leukocytes (myeloid or lymphoid), resulting in clinically identifiable cutaneous lesions.[1]Erythematous to violaceous papules and nodules are the most frequent cutaneous lesions and majority of the cases occur after the diagnosis of systemic leukemia.[1]It occurs mostly in acute myeloid leukemia(AML), in subtypes - acute myelomonocytic (AML-M4) and monocytic (AML-M5).[2] We report a case of leukemia cutis presented as plaques with haemorrhagic vesicles at the time of diagnosis of acute promyelocytic leukemia(AML-M3), which is very rare.

Case report

A 44- year -old female presented with menorrhagia since 1 month, petechiae and haemorrhagic vesicles over legs, hands and lips since 1 week, high grade fever and black colored stools since 3 days and hematemesis since 1 day. History of headache, generalised weakness and loss of appetite was present. Patient was anaemic. There was no lymphadenopathy and organomegaly.Cutaneous examination showed multiple purpuric macules, plaques with central haemorrhagic vesicle of size ranging from 1mm to 3mm involving legs, upper limbs and lips [Figures 1-3]. Genital mucosa was normal.

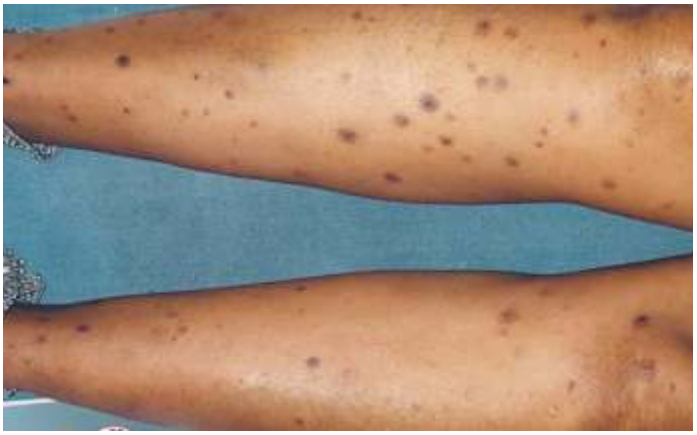

Figure 1 : Multiple purpuric macules, plaques with central haemorrhagic vesicle on both legs

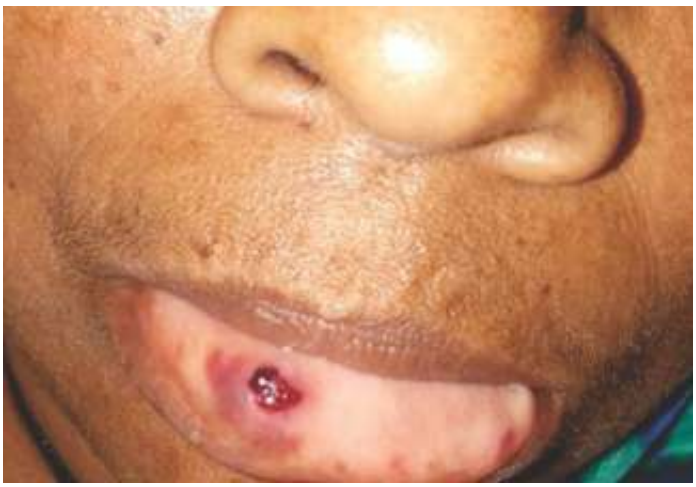

Figure 2 : Haemorrhagic vesicle on lip

Her haemoglobin was 5.6 gm/dl. Total white cell counts were raised (91,600 cells/cumm) with 92% abnormal promyelocytes/blasts.Platelets were markedly decreased (<5,000 cells/cumm). Prothrombin time was raised (19.6 seconds). Peripheral smear showed many blasts/abnormal promyelocytes with auer rods. Bone marrow aspiration showed hypercellularity with many blasts/abnormal promyelocytes.

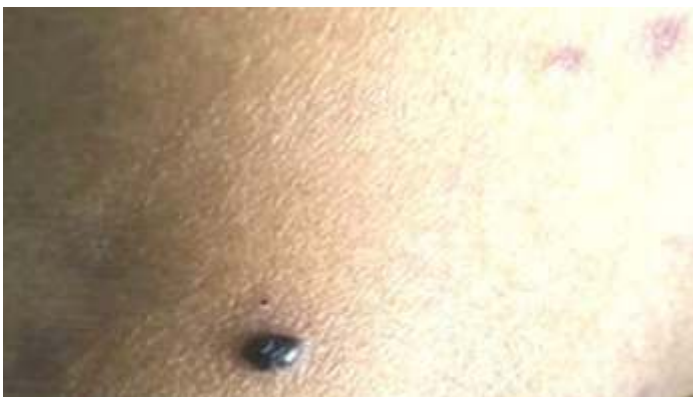

Figure 3 : Haemorrhagic vesicle on dorsal aspect of right ankle

These cells are large with pleomorphic nuclei, nuclei showing deep clefting, nuclear folds, kidney shaped nuclei. Cytoplasm is moderate with many granules. Cells with multiple auer rods (faggot cells) are also seen [Figure 4].Myeloperoxidase staining was positive. Flow cytometry revealed cells bright positive for CD33, myeloperoxidase; moderate positive for CD64,CD117; heterogenous positive for CD13; dim positive for HLA-DR; negative for B and T lymphoid antigens. These findings suggested acute promyelocytic leukemia.

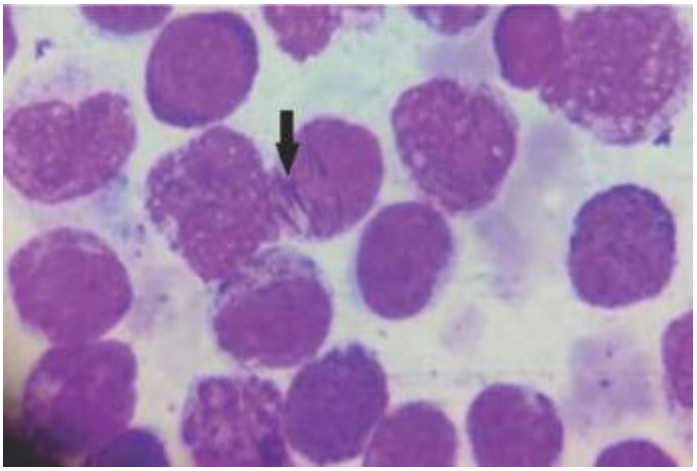

Figure 4 : Bone marrow aspiration showing abnormal promyelocytes with pleomorphic nuclei and moderate cytoplasm with many granules. Few cells with multiple auer rods are also seen (marked with arrow) (faggot cells) (Leishman stain 100 x).

Histopathology of haemorrhagic vesicle showed large subcorneal cleft filled with RBCs and leukemic cells. The leukemic cells are round to oval mononuclear cells having irregular/angulated/folded hyperchromatic nuclei with scanty to moderate dense cytoplasm. The adjoining dermis also showed infiltration by similar leukaemic cells with pagetoid involvement of epidermis [Figures 5-8].During her course in the hospital, patient was actively managed with multiple platelet transfusions, packed red cells, tranexamic acid, norethisterone, allopurinol, and all-trans retinoic acid (ATRA). Patient suddenly developed intraventricular haemorrhage after 2 days and could not be revived.

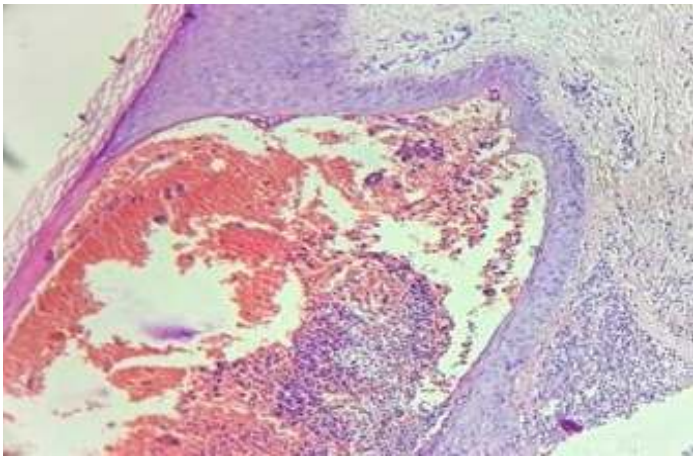

Figure 5 : Skin biopsy of haemorrhagic vesicle from the leg showing large subcorneal cleft filled with RBC's and leukemic cells with involvement of adjoining dermis by similar leukemic cells (H&E 10x)

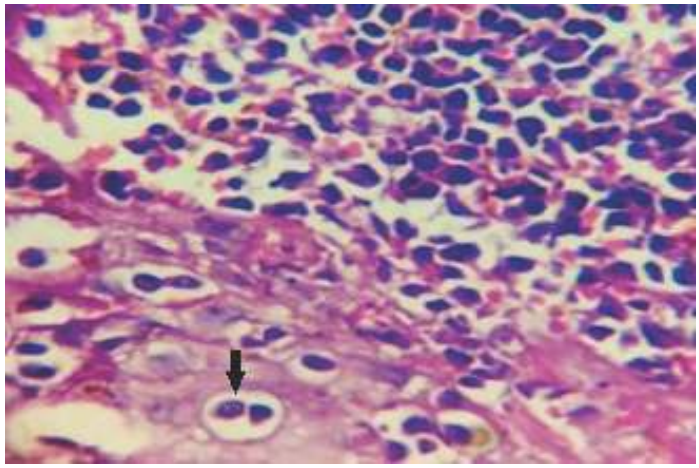

Figure 6 : Leukemic cells with pagetoid involvement of epidermis (marked with arrow) (H&E 100x)

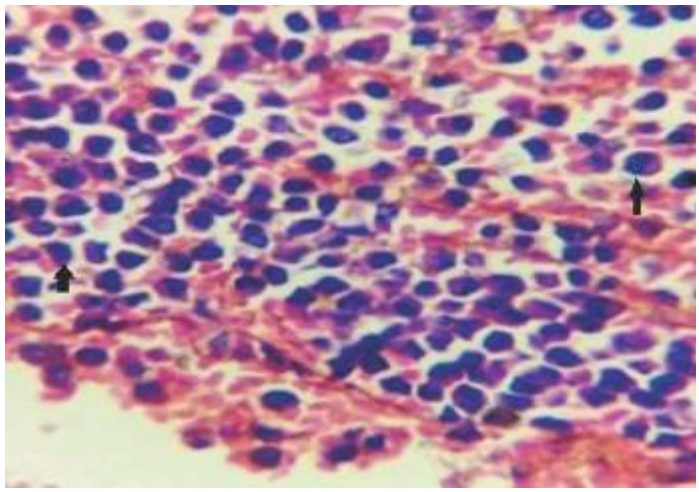

Figure 7 : Leukemic cells in the subcorneal vesicle (marked with arrows) (H&E 100x)

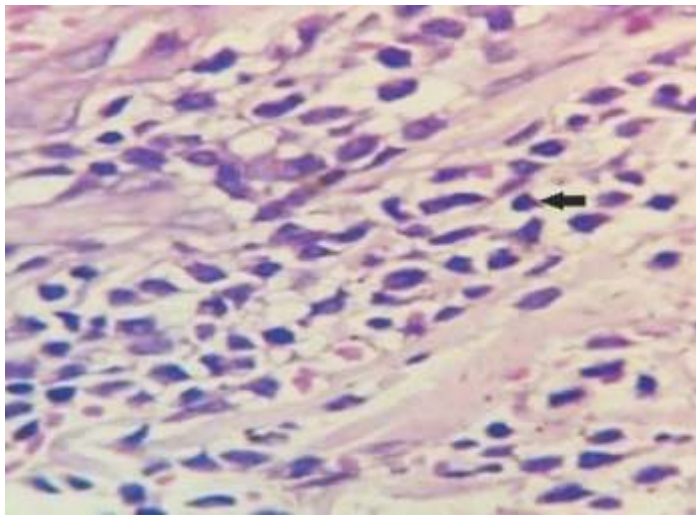

Figure 8 : Leukemic cells in dermis (marked with arrow) (H&E 100x)

Discussion

Cutaneous lesions in acute myeloid leukemia indicates grave prognosis. Without cutaneous lesions, the survival rate is 30% at 2 years, as compared to 6% in patients with cutaneous lesions.[3] Leukemia cutis in acute myeloid leukemia is rare and

the incidence ranges from 2.9 to 3.7%.[3]Mostly, leukemia cutis occurs after or in tandem with the diagnosis of systemic leukemia. Rarely, it can present prior to the involvement of bone marrow or peripheral blood and this type is termed as "aleukemic leukemia cutis or primary extramedullary leukemia". Chemokine integrin and other adhesion molecules may play a role in skin specific migration of leukemic cells.[3] Cutaneous lesions in leukemia can be specific or nonspecific [Table 1]. [3-7] Specific skin lesions are those which are characterized by leukemic infiltrates and may be diagnosed as leukemia cutis by histopathology examination, irrespective of the clinical morphology,[8] whereas nonspecific skin lesions are those that do not show leukemic cell infiltrates.

Table 1. Cutaneous lesions in leukemia

Specific lesions (leukemic cells infiltrates)	Non specific lesions (leukemids)
1. Leukemiacutis : • Erythematous to violaceous or skin colored macules, papules, plaques, nodules. (most common) • Exanthematous eruptions • Erythroderma • Purpura • Bullae and vesicles (haemorrhagic) • Ulcers • Swelling • Presenting as figurate erythemas, guttate psoriasis, vitiligo, stasis dermatitis and ulcer, seborrheic dermatitis, butterfly-like rash, leonine facies, finger tip hypertrophy, chronic paronychia, subungual leukemia cutis, sister mary joseph nodule, disseminated herpes zoster, umbilicated lesions. (unusual presentations) • Gingival hypertrophy (AML-M4 and AML-M5 • Can occur at the sites of prior or present inflammation like trauma, herpetic lesions, intravenous catheters, recent surgical sites.	1. Secondary to marrow failure: • Thrombocytopenic purpura: petechiae, ecchymosis • Infections: herpes simplex, herpes zoster, cutaneous mycoses, echthyma gangrenosum, furunculoses 2. Paraneoplastic or reactive lesions: • Chronic generalised pruritus • Pyoderma gangrenosum, Sweet's syndrome,Vasculitis • Acquired ichthyosis • Paraneoplastic pemphigus • Exfoliative dermatitis 3. Due to treatment(chemotherapy): • Drug eruptions, alopecia, stomatitis, acral erythema, neutrophilic eccrine hidradenitis, eccrine squamous syringometaplasia, graft-versus-host disease, palmar-plantar erythrodysesthesia

Skin involvement is mostly seen in acute myelomonocytic (AML-M4) and monocytic (AML-M5) subtypes of acute myeloid leukemia.Acute promyelocytic leukemia (APL), a subtype of AML is due to translocation between chromosomes 15 and 17 t(15;17)(q22;q21) and fusion between the PML gene and the retinoic acid receptor alpha gene, RARa. APL is commonly seen in adult age group and present with cytopenias, coagulopathies, and bleeding diathesis.[9] Leukemia cutis in APL is extremely rare.Only few cases of APL presenting with LC have been reported and all of them presented with LC after receiving all-trans retinoic acid (ATRA) treatment.[5]Incidence of extramedullary disease is increased in cases treated with ATRA during relapse, may be due to an increase in expression of adhesion molecules.[5] In contrast, our patient presented with lesions of leukemia cutis at the time of diagnosis and even before starting ATRA. Shvartsbeyn et al reported multiple dermatomal plaques, clinically treated as multifocal herpes zoster initially.[5]Markowski et al reported erythematous, nontender, indurated plaques with necrotic centers.[10]In both these cases, skin lesions developed before initiation of ATRA. Extramedullary involvement presenting as cutaneous lesions prior to treatment is extremely rare, which was also seen in our case.

Conclusion

In acute promyelocytic subtype, the skin lesions are very rare and most often reported after treatment with ATRA. However, in our case specific lesions with leukemic cells in epidermis and dermis are seen even before any treatment, which is again very rare. Awareness and high suspicion will help in the diagnosis of such rare cases.

How to cite this article:
Konala S, Saka S, Dantuluri P, Kolalapudi S. Leukemia Cutis in Acute Promyelocytic Leukemia: A Rare Entity. JDA Indian Journal of Clinical Dermatology 2020;3:48-50

Reference

1. Cho-Vega JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. Am J Clin Pathol. 2008;129(1):130-42.
2. Krooks JA, Weatherall AG. Leukemia cutis in acute myeloid leukemia signifies a poor prognosis. Cutis. 2018;102(4):266-71.
3. Rao AG, Danturty I. Leukemia cutis. Indian JDermatol. 2012;57:504.
4. Ramnarayanan J, Singhal S. Leukemia Cutis. eMedicineDermatology [Internet]. Web MD [updated on 2005 Jun 7 th;Cited 2010 Jan 1st]. Available from: http://emedicine.medscape.com/article/1097702-overview.
5. Shvartsbeyn M, Pandey S, Mercer SE, Goldenberg G. Leukemiacutis presenting clinically as disseminated herpes zoster in a patient with unrecognized acute promyelocytic leukemia. J Clin Aesthet Dermatol. 2012;5(4):40-43.
6. Verma P, Sharma S, Sharma R, Yadav P. Leukemia cutis manifesting umbilicated cutaneous lesions. Indian J Dermatol VenereolLeprol. 2012;78(6):752-4.
7. Grunwald MR, McDonnell MH, Induru R, Gerber JM. Cutaneous manifestations in leukemia patients. Seminoncol. 2016;43:359-65.
8. Wagner G, Fenchel K, Back W, Schulz A, Sachse MM.Leukemia cutis -epidemiology, clinical presentation,and differential diagnoses. J Dtsch Dermatol Ges.2012;10(1):27-36.
9. Araújo NS, dos Santos Júnior CJ, da Silva Gomes VM, Leite LA, Bomfim LN, da Silva Gusmão AK, Alves MJ, Romão CM, Batinga AM, da Silva MR, de Sousa Rodrigues CF. A Rare Case of Relapsed Pediatric Acute Promyelocytic Leukemia with Skin Involvement by Myeloid Sarcoma. Am J Case Rep. 2018;19:438-41.
10. Markowski TR, Martin DB, Kao GF, et al. Leukemia cutis: apresenting sign in acute promyelocytic leukemia. ArchDermatol. 2007;143(9):1220–1221.