International Journal of Advances in Medicine
Singh A et al. Int J Adv Med. 2021 Feb;8(2):293-296
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20210280

Case Report

Monocytic leukeima masquerading as a cutaneous lesion

Abhishek Singh, Shifa Farheen, Preeti Tripathi*, Arijit Sen, Akriti Kashyap

Department of laboratory Medicine, Command Hospital Airforce, Bangalore, Karnataka, India

Received: 02 December 2020
Revised: 10 January 2021
Accepted: 11 January 2021

***Correspondence:**
Dr. Preeti Tripathi,
E-mail: contactdoctorpreeti@gmail.com

ABSTRACT

Cutaneous lesions preceding a leukaemia are extremely rare and are referred to as 'aleukaemic leukaemia cutis'. We present a case of acute monocytic leukaemia where skin infiltration of leukemic cells preceded any blood or bone marrow evidence of leukaemia. A 67-year-old woman presented with multiple cutaneous nodules all over the body of 3 months duration. Cutaneous examination showed multiple erythematous papules and plaques which were present over the face, trunk, extremities and back. Patient was evaluated at a nearby facility and was found to have normal blood parameters (TLC- 7130/cmm, N-57% L-34% M-09%). A skin biopsy done revealed infiltration of the dermis by atypical cells suggestive of a hematolymphoid malignancy. The patient was then shifted to our institution for tertiary care management. The blood counts over a period of one month showed gradually increasing TLC from an initial normal blood count to one showing absolute monocytosis (TLC-25500/cmm, AMC-3825/cmm) and finally abnormally high TLC (TLC-154050/cmm) with 79% monoblasts and promonocytes suggestive of acute leukaemia. A repeat skin biopsy again showed infiltration of atypical cells in the dermis. IHC done showed the atypical cells to be positive for monocytic markers (CD14, CD64). The patient had now started exhibiting systemic findings corroborating with the cutaneous lesions and skin biopsy. Bone marrow aspirate was hypercellular and showed replacement by monoblasts (82%). Cellular morphology was suggestive of AML-M5. Bone marrow biopsy showed a diffuse replacement of marrow by immature cells/blasts. Flow cytometry reports were also positive for monocytic markers. The patient was hence diagnosed as AML M5 with cutaneous metastasis/leukemia cutis and was immediately started on chemotherapy (3+7). Post induction phase, the patient was in remission and her skin lesions subsided. She was subsequently discharged and advised regular OPD follow up for maintenance therapy. This case is reported for its rarity.

Keywords: Leukaemia cutis, Monoblasts, Flow cytometry

INTRODUCTION

Leukemia cutis is the presence of atypical leucocytes or leucocytic precursors into the epidermis, dermis, or subcutaneous tissue, resulting in clinically distinguishable cutaneous lesions. Leukaemia cutis is a broad term used to describe any cutaneous demonstration of leukaemia which may recede, succeed or occur simultaneously with the diagnosis of leukaemia. The pathologist is instrumental in the diagnosis of leukaemia cutis. It is a diagnostic challenge, resolved by prudent immunophenotyping and cytochemistry. Accurate diagnosis has incredible prognostic importance. It may help establish a diagnosis in cases in which leukaemia cutis heralds the process of systemic leukaemia. A diagnosis of leukaemia cutis generally augurs a poor prognosis and strongly correlates with additional sites of extramedullary involvement.[1] The prevalence of 2.9–3.7% of AML cases have been noted to present with leukaemia cutis. Acute myelomonocytic leukaemia (AML M4) and (AML M5) have the maximum incidence of presentation of cutaneous lesions amongst all the FAB subtypes and has been recorded as high as 30 50%.[2-5] In majority cases of leukaemia cutis, the patients have a preexisting systemic disease. In as many as 7% of patients, leukaemia Cutis precedes bone marrow or blood involvement.[6]

CASE REPORT

A 67-year-old female, a known case of depressive disorder, type 2 DM, hypertension on regular medications. The lady presented with complaints of erythematous papules and nodules over her body for the last 03 months (Leg lesions-Figure 1a). These lesions started over the face and progressed to involve the entire body. A history of easy fatiguability with occasional breathlessness was present. There was no history of itching, night sweats, weight loss, fever or bleeding manifestation. The patient gave no history of smoking or alcohol intake. On general examination, pallor was present. There was no icterus, lymphadenopathy or hepatosplenomegaly. Oral cavity showed Gingival hyperplasia (Figure 1b). On dermatological examination, multiple well to ill defined, discrete to coalescent erythematous papules and plaques were present over the face, trunk, extremities and back. There was no sensory deficit and no nerve thickening. Patient was evaluated in a hospital in her hometown initially where she was found to have normal blood parameters (TLC- 7130/cmm, N-57% L-34% M-09%). A skin biopsy done revealed infiltration of the dermis by atypical cells suggestive of a hematolymphoid malignancy. A repeat cbc after a week showed normal counts again (TLC-9780/cmm, N-55%, L-32% M-12%). The patient was then shifted to our institution for tertiary care management. Blood counts showed a gradual increase from normal counts initially to elevated TLC (25500/cmm) with absolute monocytosis (absolute monocyte count-3825/cmm) (Figure 2a).

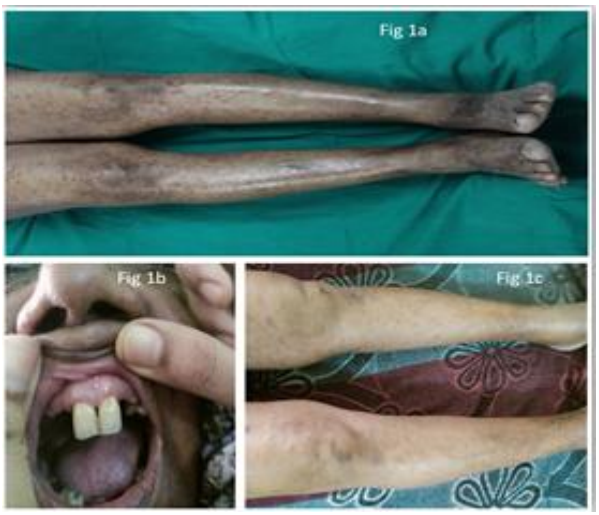

Figure 1: (a) erythematous macules and papules on the lower limb of the patient (b) gingival hyperplasia- another marker of monocytic leukemia (c) shows the lesions having subsided post induction phase chemotherapy.

A complete work up of the patient was done. 2D echo, chest X ray and abdominal USG showed normal findings. Whole body PET scan revealed multiple mildly avid sub centimetric clavicular lymph nodes, tiny nodular lesion in the subcutaneous plane in lower limb and mildly increased marrow uptake in both femur and humerus. A Skin biopsy was repeated from one of the erythematous papules. Histopathological examination of the skin biopsy showed normal epidermis with preserved grenz zone. Dermis showed atypical cells arranged in diffuse sheets and in a perivascular and periadnexal pattern–suggestive of cutaneous metastasis (Figure 3a). IHC done was positive for monocytic markers (CD14 and CD64). Subsequently, blood investigations revealed an abnormally high total leucocyte count (TLC-154050/cmm) with 79% monoblasts and promonocytes suggestive of acute leukemia.

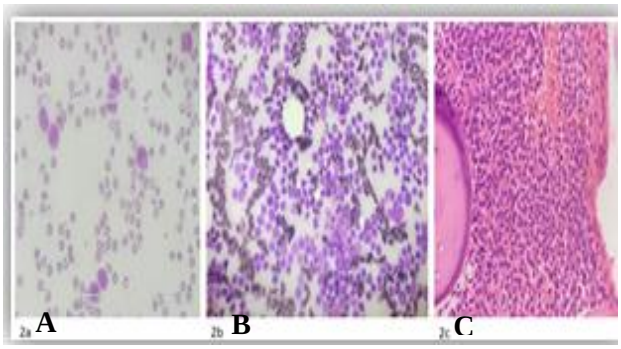

Figure 2: (A) shows a photmicrograph (40x) exhibiting Absolute Monocytosis (B) shows a bone marrow aspirate showing complete replacement by monoblasts (C) exhibits a diffuse replacement of bone marrow by immature cells/blasts.

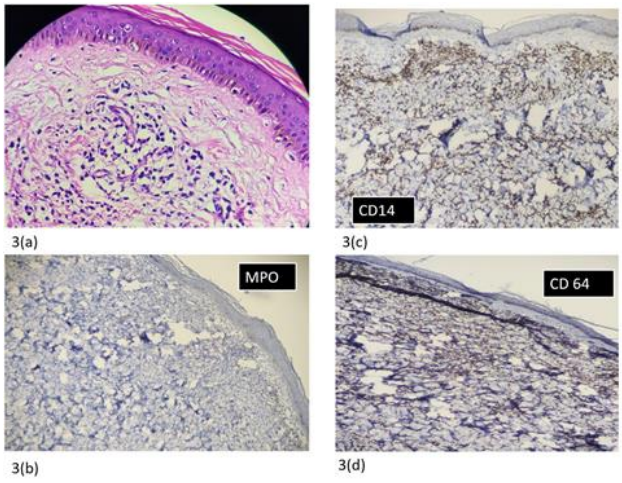

Figure 3: (a) photomicrograph of a skin biopsy depicting an infiltration of the dermis by atypical cells suggestive of a hematolymphoid malignancy. (b, c, d) IHC done on the skin biopsy to be positive for CD 14 , CD 64 and negative for MPO.

The patient was now exhibiting systemic findings corroborating with the cutaneous lesions and skin biopsy. Bone marrow aspirate was hypercellular and showed replacement by monoblasts (82%) (Fig 2b). Cellular morphology was suggestive of acute monoblastic

leukemia as per the WHO 2016 classification of haematolymphoid malignancy. Bone marrow biopsy showed a diffuse replacement by immature cells/blasts again suggestive of acute leukemia (Figure 2c). Flow cytometry markers were negative for immature markers like HLADR and MPO and showed positivity (Figure 3b) for monocytic markers like CD13, CD14, CD56 and CD64 which confirmed the diagnosis of AML-M5 (Figure 3c and 3d). Molecular studies were negative for any mutation suggestive of a chronic myeloproliferative disorder (negative for JAK2V617F, JAK2 EXON12, MPL EXON 10, CALR EXON9 mutation and BCR/ABL1 translocation). The patient was hence diagnosed as AML M5 with cutaneous metastasis/leukemia cutis and was immediately started on chemotherapy (3+7 chemotherapy). Post induction phase, the patient was in remission and her skin lesions subsided (Figure 1c). She was subsequently discharged and advised regular OPD follow up for maintenance chemotherapy.

DISCUSSION

The incidence of leukaemia cutis is thought to be between 2.9 and 3.7% for acute myeloid leukemia (AML).[7] Of these cases, 7% present as aleukemic leukemia cutis.[8] The majority of leukemia cutis occurs with a concomitant presentation of systemic leukaemia (23-44%) or in the case of a patient with an already established leukaemia (44-77%). Rarely, leukaemia cutis can precede the development of discernible leukaemia in the peripheral smear and/or marrow.[9] A few genetic abnormalities are seen with leukaemia cutis eg translocation (8;21) (q22;q22), and inversion (16) (p13; q22).[8,10] The understanding of the specific migration of leukemic cells to the skin is not clear. It is postulated that cell adhesion molecules like chemokines and integrin may play an important role in skin specific infiltration of T and B leukemic cells. Leukaemia cutis is related with a higher incidence of extra medullary leukemic involvement. The CNS localization of AML occurs most commonly in patients with leukaemia cutis (17%).[11] Cutaneous involvements of leukaemia can be specific (infiltrates of leukemic cells) or nonspecific (paraneoplastic, inflammatory, or secondary to marrow failure). Leukaemia cutis is basically a distinct sign of systemic leukaemia and is the result of migration of leukemic cells to the skin. The clinical appearance of leukaemia cutis is highly variable with nodules or erythematous to violaceous papules being the most commonly seen lesions (60%), followed by infiltrated plaques, erythroderma and generalised cutaneous eruption. They are mostly asymptomatic and are not associated with any pruritis.[12] The nodules are mostly firm or rubbery in consistency, and can turn itchy or purpuric if the patient has thrombocytopenia. The reported case also presented with asymptomatic generalized erythematous plaques and nodules. Unusual presentations are those resembling stasis dermatitis, guttate psoriasis and ulcerate lesions. There are also case reports of leukaemia cutis seen at sites of herpetic lesions, i.v lines and recent surgeries. Nonspecific cutaneous involvement of leukaemia is much more common, occurring in up to 30-40% of patients. The paraneoplastic conditions are seen with generalized pruritus, Sweet's syndrome, urticaria, erythema multiforme, erythema nodosum, ichthyosis, pyoderma gangrenosum, exfoliative dermatitis and vasculitis. The most common nonspecific signs are haemorrhagic, including purpura, petechiae and ecchymosis. There is also an increased incidence of drug eruptions in patients with leukaemia. Incidence of AML is higher in men. However, the reported case is a female. Heredity, radiation, occupational chemical exposure and drugs have all been incriminated in the development of AML. No such history was reported in our case. Acute myelomonocytic leukaemia (AML-M4) and (AML-M5) have the highest rates of cutaneous involvement amongst all the subtypes and are reported to be as high as 30%. Most patients of AML present with nonspecific symptoms. Significant haemorrhage occurs in acute promyelocytic leukaemia. Infiltration of gingivae, skin or meninges is characteristic of monocytic subtypes (AML-M4 and AML-M5). Gingival hyperplasia is seen in 42% of AML-M5 and 55% of AML-M4.[12]

Our case also had gingival hyperplasia, which is expected in AML-M5. A thorough work up of the patient is crucial for the diagnosis of the specific type of leukaemia. More than 20% blasts in the peripheral blood is suggestive of acute leukaemia. Skin biopsy along with immunohistochemistry is necessary to determine the immunophenotype of leukemic cells seen infiltrating the dermis. Flow cytometry is important for confirming the diagnosis of leukaemia. Elevated LDH is seen in patients with leukaemia cutis and considered as a sign of poor prognosis.[8] Current treatment involves chemotherapy. The various antineoplastic agents used in the treatment of AML are Daunorubicin, Idaurubicin, Cytarabin, Tretinoin, Gemtuzimab, Etoposide and methotrexate. Radiotherapy is considered to be beneficial in widespread skin involvement; a higher incidence of skin relapses indicates that skin acts as a sanctuary for leukemic cells.[11]

Whole-body electron-beam radiation has emerged as a valuable alternative to conventional irradiation, preventing systemic toxicity. The prognosis is poor, as many patients end up with extramedullary disease and poor survival rates. Most patients die within months of diagnosis. Patients with AML without skin lesions have a survival rate of 30% as compared to 6% in patients of AML with skin lesions indicating a grave prognosis of leukemia cutis.[13] Our patient has shown a good response to induction chemotherapy and her skin lesions have diminished. She has been advised regular OPD follow up for maintenance chemotherapy.

CONCLUSION

Cutaneous infiltration before systemic signs of leukaemia is a fairly rare occurrence. However, an early diagnosis specially preceding multisystem involvement will go a

long way in improving the prognosis and survival rate of the patient.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Cho-Vega JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. Am J Clin Pathol. 2008;129:130-42.
2. Wagner G, Fenchel K, Back W, Schulz A, Sachse MM. Leukemia cutis-epidemiology, clinical presentation, and differential diagnoses. J Dtsch Dermatol Ges. 2012;10:27-36.
3. Vishalakshi V, Torsekar RG, Shinde S. Aleukemic leukemia cutis. Indian J Dermatol Venereol Leprol. 2007;73:109.
4. Ohno S, Yokoo T, Ohta M, Yamamoto M, Danno K, Hamato N, et al. Aleukemic leukemia cutis. J Am Acad Dermatol 1990;22 (2 Pt 2):374-7.
5. Yoder FW, Schuen RL. Aleukemic leukemia cutis. Arch Dermatol 1976;112:367-9.
6. Cho Vega JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. Am J Clin Pathol 2008;129:130-42.
7. Yones SS, Khorasgani MG, Iqbal T, Arrifin N, Mehta R, Skibinska G, et al. Aleukemic leukemia cutis. Egypt Dermatol Online J 2009;5:1-8
8. Agis H, Weltermann A, Fonatsch C, Haas O, Mitterbauer G, Móllauer L, et al. A comparative study on demographic, haematological and cytogeentic findings and prognosis in acute myeloid leukaemia with or without leukemia cutis. Ann Hematol 2002;81:90-5
9. Yones SS, Khorasgani MG, Iqbal T, Arrifin N, Mehta R, Skibinska G, et al. Aleukemic leukemia cutis. Egypt Dermatol Online J 2009;5:1-8.
10. Kubonishi I, Seto M, Murata N, Kamioka M, Taguchi H, Miyoshi I. Translocation (10;11) (p13;q13) and MLL rearrangement in a case of AML (M5a) with aggressive leukemiacutis. Cancer Genet Cytogenet 1998;104 (Suppl 1):28-31.
11. Zweegman S, Vermeer MH, Bekkink MW, van Der Valk P, Nanayakkara P, Ossenkoppele GJ. Leukemia cutis: Clinical features and treatment strategies. Haematologica. 2002;87-90
12. Koizumi H, Kumakiri M, Ishizuka M, Ohkawara A, Okabe S. Leukemia cutis in acute myelomonocytic leukemia: Infiltration to minor traumas and scars. J Dermatol. 1991;18:281-5.
13. Ramnarayanan J, Singhal S. Leukemia cutis. E medicine dermatology. Web MD. Available from: http://emedicine.medscape.com/article/1097702-overview. Accessed on 20 July 2020.

Cite this article as: Valekar SS, Kshirsagar V, Ashturkar MD, Mhaske M, Chawla PS, Fernandez K. Monocytic leukeima masquerading as a cutaneous lesion. Int J Adv Med 2021;8:293-6.