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Leukemia Cutis with Acute Myelomonocytic Leukemia Presenting As a Benign Appearing Maculopapular Rash: A Rare and Interesting Case Report

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ABSTRACT
A 54 years old male came with the complaints of raised multiple maculopapular lesions involving the forehead and lateral side of the nose. Skin biopsy showed thinning of epidermis and diffuse monomorphic population of infiltrate involving the dermis and subcutis with round nuclei, high NC ratio and scanty cytoplasm. Complete Haemogram showed low haemoglobin (4.3g/dl), leukocytosis (total count: 43,400/microliter) and marked thrombocytopenia (platelets: 36,000/microliter). Peripheral blood picture revealed acute leukemic picture with 45% myeloblasts and 46% of monocytes and its precursors. It was confirmed as Leukemia cutis with acute myelomonocytic leukemia by further bone marrow aspiration study and immunohistochemistry.
Keywords: *Leukemia cutis, bone marrow aspiration, Immunohistochemistry.*

INTRODUCTION

Infiltration of the skin by malignant neoplastic leucocytes or their precursors is called as Leukemia cutis and it can involve epidermis, dermis or sub cutis resulting in clinically detectable benign or malignant appearing skin lesions.(1) Cutaneous involvement of leukemia can be seen when there is infiltration of skin by bone marrow derived leukemic cells with chromosomal as well as maturation aberrations. Rarely does it become the first presentation but it is more commonly coexisting with the primary leukemia and manifests as a diffuse infiltration. Though it can be seen in various types of leukemia namely chronic myeloid and lymphoid as well as acute myeloid, the more common entity is acute myeloid leukemia (AML) of M4 and M5 type from French American British (FAB) classification. (2)

Approximately 10-15% of AML patients develop leukemia cutis. Aleukemic leukemia cutis is defined as skin infiltration in the absence of bone

marrow involvement, which is a rare entity and proved to have poor prognosis.[3]

CASE REPORT

A 54 years old male came to dermatology outpatient department without any significant prior medical history, complaints of raised multiple maculopapular lesions involving the forehead and lateral side of the nose, abruptly developed ten days earlier which was associated with intermittent moderate fever, loss of weight , loss of appetite and easy fatigability for the past one week.

On general examination, he was thin built, ill-nourished and pale. Dermatologic examination revealed multiple varying sized nontender violaceous maculopapular skin lesions with irregularly indurated margins on face [Figure 1a]. Systemic examination showed normal vitals and mild splenomegaly on palpation which is also confirmed by abdominal ultrasonogram.

Skin punch biopsy of the lesion was performed and was submitted to histopathology lab with clinical diagnosis of urticarial vasculitis, drug induced dermatitis and erythema nodosum. Skin biopsy showed thinning of epidermis and diffuse monomorphic population of infiltrate involving the dermis and subcutis with round nuclei, high NC ratio and scanty cytoplasm. The infiltrates were arranged in sheets and linear cords percolating between the dermal collagen bundles and adnexal structures [Figure 1b & c]. Since the patient complained about high fever, peripheral smear examination and complete blood count were sent simultaneously to laboratory.

His hemogram showed low haemoglobin (4.3g/dl), leukocytosis (total count: 43,400/micr-oliter) and marked thrombocytopenia (platelets: 36,000/microliter). Peripheral blood picture revealed acute leukemic picture with 45% myeloblasts and 46% of monocytes and its precursors. [Figure 2a, b & c]. Subsequently bone marrow aspiration was done which showed 40% myeloblasts and 30% of monocytes and precursors. [Figure 2d] Erythropoiesis and megakaryopoiesis were suppressed. Smear was reported as acute myelomonocyticleukemia FAB – M4 subtype.

Further immunohistochemistry evaluation of cutaneous infiltrate revealed immunopositivity for myeloperoxidase (focal), strong diffuse positivity of CD 45 as well as CD68 [Figure 3a & b] and immunonegative for the markers CD 117 and CD 34. [Figure 3c] Findings were consistent with Leukemia cutis by Myelomonocytic leukemic cells.

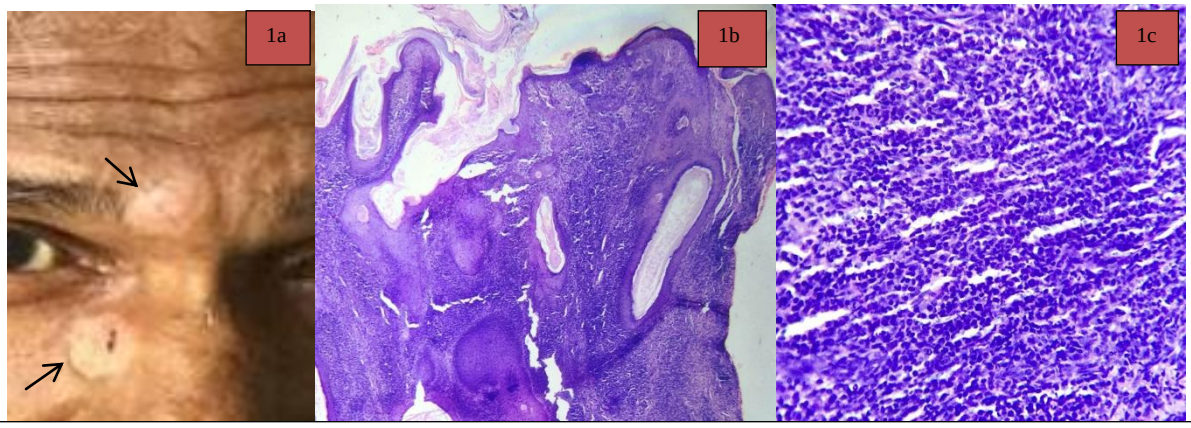

Figure 1a – infiltrating indurated maculopapular rash in the face, **1b** – skin biopsy with diffuse monomorphic leukemic infiltrate [H&E, 40X], **1c-** Diffuse array of cells percolating through dermal collagen fibres [H&E, 100X]

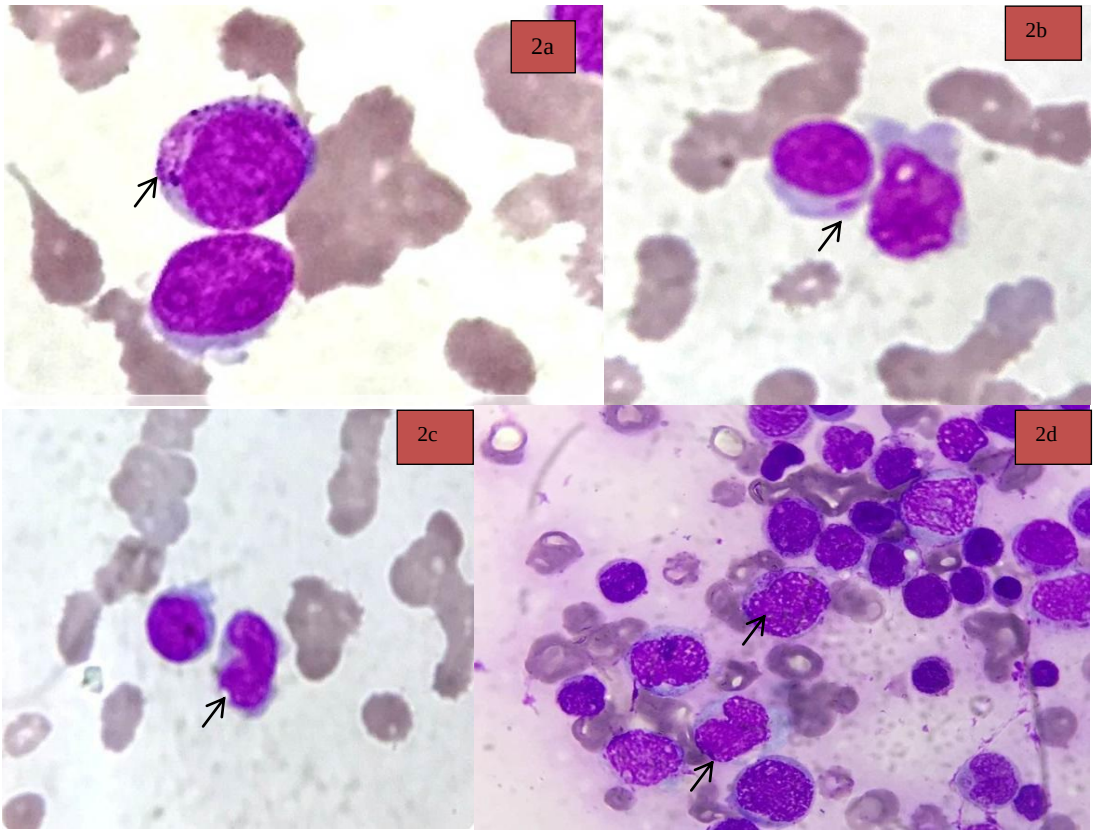

Figure 2 – a,b,c Peripheral smears with myeloblasts with granules **[2a]** and auer rod **[2b]** and monoblast with cytoplasmic vacuoles **[2c]** (Leishman stain 1000X),2d shows bone marrow aspiration picture with myeloblast, monoblast and erythroblasts (Leishman stain 1000X)

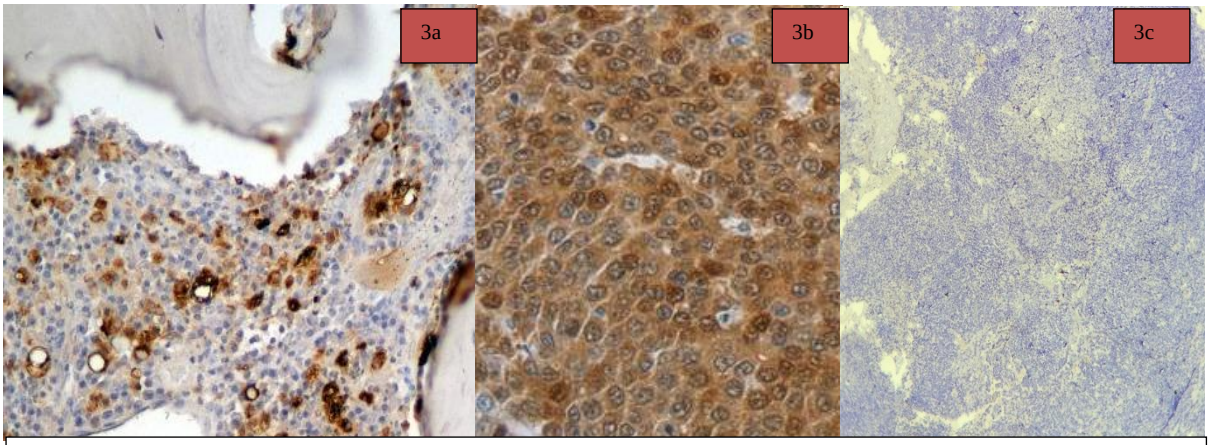

Figure 3- IHC profile -CD68 strong positivity in monocytic infiltrate (100X), **b-** CD 45 diffuse strong nuclear and cytoplasmic positivity in tumour cells (400 X**), c –** CD117 tumour cells show diffuse immunonegativity (40X)

DISCUSSION

AML characteristically shows atypical myeloid or myelomonocytic precursors in the peripheral blood and bone marrow resulting in mild to severe degrees of anemia and usually associated with significant amount of thrombocytopenia. Cutaneous infiltration by AML is a rare initial presentation but it is more commonly diagnosed as a late manifestation of widespread or advanced infiltrative leukemia. The common sites of involvement are head, neck and trunk region. In our case it involved face. Epidemiologic variations are commonly encountered in various types of leukemia, for example ALL occurs

usually in children, AML as well as CML occurs in adults and CLL commonly seen in elderly age group [4]

The clonal expansion of leukemic infiltrate is the result of oncogene activation, tumor suppressor gene inactivation and abnormality in differentiation along with decreased apoptotic potential. [5] The prognosis when it occurs in younger patients is poor as shown in previous literature. [6]

The WHO classification defines acute leukemia as minimum of 20% of blasts cells in the peripheral blood or bone marrow, however FAB classification recommends minimum of 30% of blast cells, our case had more than 90% of blasts in the peripheral blood, thus fulfilling the WHO criteria. [7] Subtyping of leukemias are important for prognostic assessment and to implement individualized therapeutic protocol. Cytochemistry, immunophenotyping by flow cytometry or immunohistochemistry (IHC) are required for subtyping. In our case leukemic cells in tissue biopsy was positive for IHC markers myeloperoxidase (MPO) and CD 68 a monocyte macrophage marker, proving both myeloid and monocytic origin which is consistent with peripheral smear morphological findings. IHC markers CD117 and CD34 were found to be negative in our case excluding other close differentials like small round blue cell tumours and undifferentiated tumors. Leukemia cutis is more commonly seen with acute monocyticleukemia (10-33%) and myelomonocytic leukemia (13-23%) M5 and M4 of FAB classification.[8]

A multiparametric approach including histomorphologic features in blood smear and tissue biopsy, cytochemical analysis as well as immunophenotyping by Immunohistochemistry or flow cytometry are often necessary to conclude definite diagnosis and exclude from closer morphological differential diagnosis like large cell lymphoma and poorly differentiated carcinoma.

Leukemia cutis often presents with nonspecific symptoms like widespread purpura, pruritic macules, infiltrating erythematous nodules or papules along with symptoms of cytopenia as pallor, infections and varying degrees of bleeding manifestations. Hence clinical suspicion is at most important for further hematological workup and definite diagnosis. Since prognosis of leukemia cutis is poor, early accurate diagnosis, subtyping by applying appropriate immunophenotype markers and individualized aggressive treatment protocol are mandatory for better clinical outcome.

CONCLUSION

Our case Leukemia cutis with underlying acute myelomonocytic leukemia presenting as benign skin maculopapular rash is a rare presentation with poor prognosis. Hence, it is a diagnostic challenge for `clinicians as well as pathologists and requires high degree of suspicion for further work up and better prognosis.

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