Aleukemic leukemia cutis mimicking urticaria pigmentosa in a patient of T-cell acute lymphoblastic leukemia

Sir,

A 24-year-old woman presented with progressively increasing itchy, erythematous lesions on the face, trunk and arms since the past 6 months. She also complained of a slight reduction in appetite with mild constitutional symptoms, viz., malaise and early fatigue of 15 days' duration. On examination, there was predominant involvement of malar area and lateral part of the cheeks, trunk and both arms with multiple erythematous to brownish macules and plaques ranging from 0.5 to 3 cm in size [Figure 1a]. The Darier's sign was strongly positive in the lesional skin [Figure 1b]. Generalized lymphadenopathy with involvement of cervical, axillary and inguinal areas was present. With a clinical diagnosis of adult-onset mastocytosis, complete blood counts, serum trypsin levels and peripheral blood smear were evaluated, which were within normal limits. Skin biopsy on hematoxylin and eosin staining showed a pan-dermal dense infiltrate of lymphocytes and histiocytes, with few atypical lymphocytes [Figure 2a]. Mast cells were absent and this finding was confirmed with Giemsa and toluidine blue staining. Four weeks after the initial visit, the complete blood count and peripheral blood smear were repeated, which revealed lymphocytosis (60%) along with some atypical cells in peripheral blood smear. A bone marrow biopsy was performed, which showed multiple, large atypical cells [Figure 3a]. These cells showed negative staining for the markers of myeloid lineage, i.e. myeloperoxidase, Sudan black B and nonspecific esterase [Figure 3b and c]. Immunophenotyping by flow cytometry showed positivity with CD3, CD5, CD7 and terminal deoxynucleotidyl transferase. Immunohistochemical staining of skin biopsy with CD3 and terminal deoxynucleotidyl transferase also revealed positive staining, suggesting the origin of lymphocytes being of T-cell lineage [Figure 2b and c], thus confirming the diagnosis of leukemia cutis masquerading as adult-onset mastocytosis with T-cell acute lymphoblastic leukemia. Leukemia cutis was further designated as aleukemic leukemia cutis because cutaneous involvement preceded the deranged hematological profile. The patient was referred to the hemato-oncology unit for further management, and was started on augmented Berlin-Frankfurt-Munster therapy for acute lymphoblastic leukemia. After consolidation phase of chemotherapy, the patient had flattening of her lesions and the erythematous lesions gradually turned hyperpigmented.

Leukemia cutis is defined as a cutaneous infiltration of leukemic cells, and is an extramedullary manifestation of underlying leukemia. It is observed more frequently in acute myeloid leukemia, particularly in myelomonocytic (M4) and monoblastic (M5) subtypes.[1] Cutaneous involvement in acute lymphoblastic leukemia is uncommon with an incidence ranging from 1 to 3%.[2] Furthermore, its T-cell variant rarely presents as leukemia cutis. The commonest cutaneous presentation of leukemia cutis is that of asymptomatic, indurated papules and nodules.[3] Macules, maculopapular lesions, plaques, ulcers, bullae, large nodule, ecchymosis, palpable purpura and erythroderma are uncommon presentations.[1,3] The lower extremities are the most commonly involved site followed by the upper extremities, trunk, scalp and face.[2,4] Leukemic changes in peripheral blood or bone marrow usually develop before skin involvement. Occasionally, leukemia cutis precedes the diagnosis of systemic leukemia by several months or even years (mean 6 months).[5] This interesting condition is known as aleukemic leukemia cutis. T-cell acute lymphoblastic leukemia presenting as aleukemic leukemia cutis is rarely described in the literature [Table 1]. There is relative paucity of literature with regards to this clinical presentation on the overall prognosis; nonetheless, reports of a poor outcome do exist.[1,4] Association of urticaria pigmentosa-like lesions with acute lymphoblastic leukemia has been described previously in case reports.[6]

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Table 1: Previously reported cases of aleukemic leukemia cutis in T-cell acute lymphoblastic leukemia

Authors	Age/ sex	Morphology of cutaneous lesion	Sites of involvement	Latency period between cutaneous and hematological involvement	Treatment	Outcome
van Zuuren *et al.**	33Y/F	Brown-purple plaque Rubbery nodules	Right lower extremity Left flank	2 years	Radiotherapy for cutaneous lesions and allogenic BMT after chemotherapy	CR after BMT.
Ali *et al.*	16Y/F	Maculopapular lesions Reddish-purple mass	Generalized Right anterior femoral region	3 months	Chemotherapy (Vincristine, Prednisolone Cyclophosphamide, Daunorubicin, L-asparaginase)	CR
Najem *et al.*	8Y/M	Multiple erythematous and purpuric nodules Erythematous macules and nodules Large crusted ulcers	Both shins Widespread Right knee and both buttocks	6 months	Referred to cancer control center	-
Shahriari *et al.**	8Y/M	Hard palate and gum hypertrophy Erythematous maculopapular rash	Oral cavity Face and trunk	-	Standard T-cell ALLprotocol	Both types of lesions improved two weeks after chemotherapy
Current Case	24Y/F	Multiple erythematous to brownish macules and plaques with Darier's sign positivity	Trunk, malar area, lateral part of the cheeks and both arms	7 months	Augmented and standard Berlin-Frankfurt-Münster chemotherapy regimen	After 1st cycle, significant flattening of skin lesions

*Aleukemic leukemia cutis presenting as relapse in previously treated cases. Y: years, M: male, F: female, BMT: Bone marrow transplant, CR: Complete remission, ALL: Acute lymphoblastic leukemia

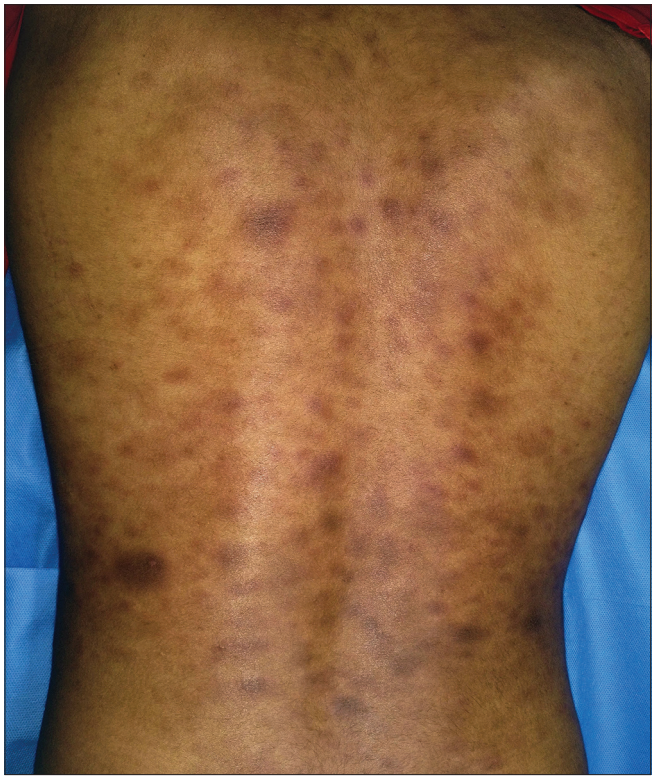

Figure 1a: Multiple, discrete, erythematous to brown macules and plaques on back

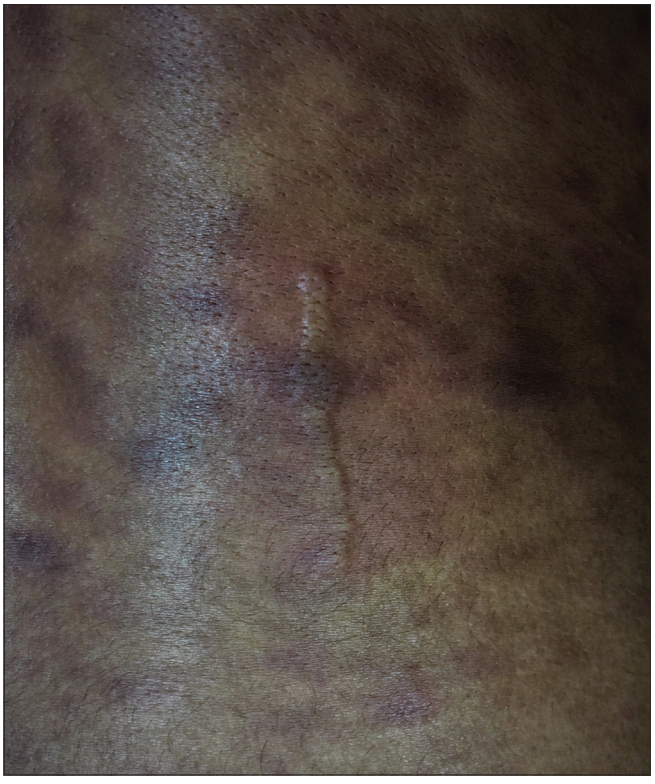

Figure 1b: Positive Darier's sign in plaque on lower back

In the classical Darier's sign, local itching, erythema and wheal formation occur within 2–5 minutes of gentle rubbing or stroking of the cutaneous lesions. It is considered to be pathognomonic of cutaneous mastocytosis; however, it is seen uncommonly in various other dermatological

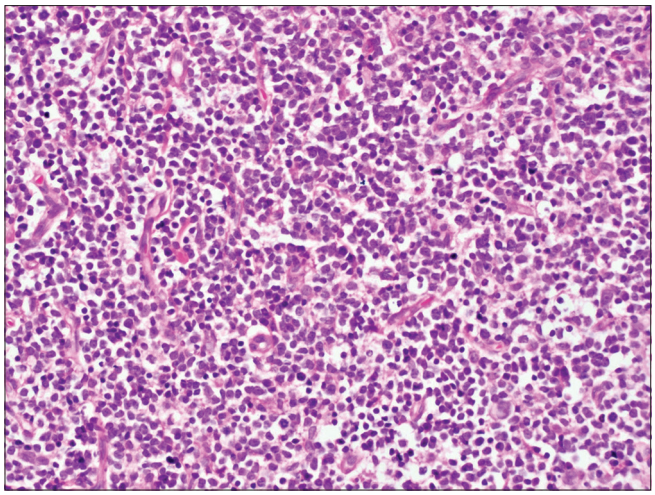

Figure 2a: Dense lymphocytic infiltrate in the dermis with few atypical lymphocytes (×400)

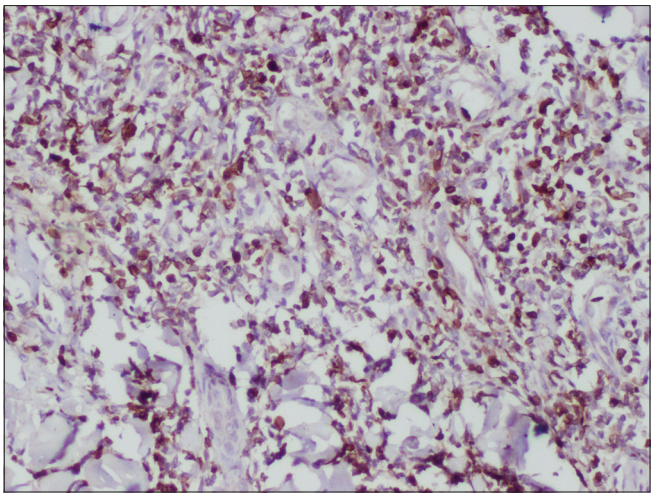

Figure 2b: CD3 positivity on immunohistochemical staining of skin biopsy specimen (×400)

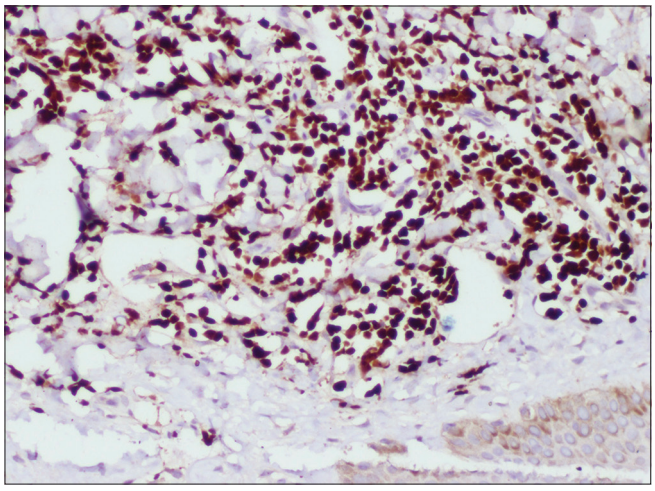

Figure 2c: TdT positivity on immunohistochemical staining of skin biopsy specimen (×400)

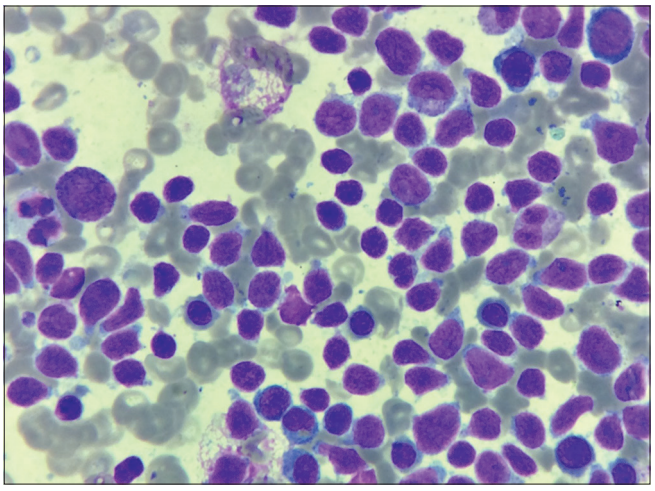

Figure 3a: Bone marrow biopsy showing multiple large lymphoblasts (×1000)

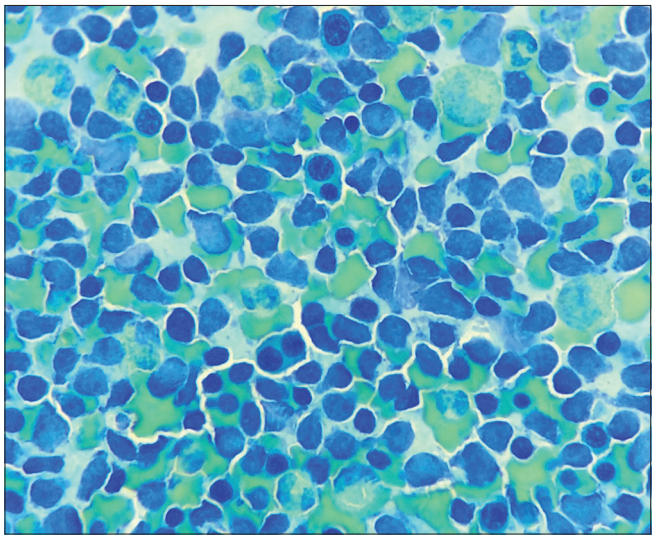

Figure 3b: Negative staining with myeloperoxidase (×1000)

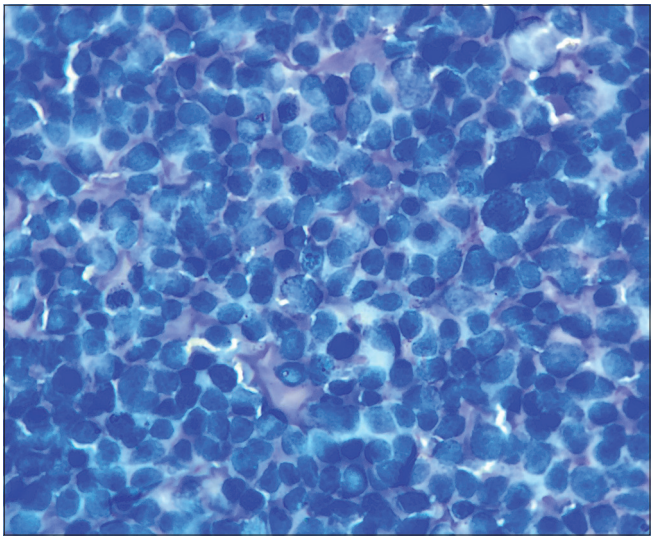

Figure 3c: Negative staining with Sudan black B (×1000)

disorders such as leukemia cutis, juvenile xanthogranuloma, Langerhans cell histiocytosis and cutaneous large T-cell lymphoma.[7] As far as ascertained, our case is the first case of aleukemic leukemia cutis with the Darier's sign positivity, mimicking as urticaria pigmentosa, in a patient of T-cell acute lymphoblastic leukemia.

In conclusion, T-cell acute lymphoblastic leukemia rarely leads to leukemia cutis and furthermore, aleukemic leukemia cutis and dermatologic presentation masquerading as urticaria pigmentosa is very uncommon.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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