Hypopigmented and acneiform lesions: An unusual initial presentation of adult-onset multisystem Langerhans cell histiocytosis

Dear Sir,

Langerhans cell histiocytosis is a rare neoplasm of Langerhans cells.[1] Its incidence in pediatric population is 4–5 per million, whereas incidence in adults is approximately one-third of this.[2] The cutaneous involvement in adult-onset Langerhans cell histiocytosis commonly encountered in association with multisystem disease. Isolated cutaneous Langerhans cell histiocytosis is rare. Heterogeneous cutaneous manifestations, such as intertrigo, perianal erosions, centrofacial fleshy plaques and prurigo-like nodules, have been described in both multisystem and isolated cutaneous variants of adult-onset Langerhans cell histiocytosis.[3,4] Here, we describe two adult patients presenting with hypopigmented and acneiform lesions finally being diagnosed as multisystem Langerhans cell histiocytosis.

Case 1: A 35-year-old man presented with multiple, discrete, 2–3 mm, nonscaly, hypopigmented to depigmented macules on the back which were noticed recently [Figure 1a]. He also had recalcitrant papulopustular lesions with crusting on scalp for 5 years [Figure 1b] and nail dystrophy [Figure 1c]. Several finger and toenails had thickening, discoloration, paronychia and onychorrhexis. Potassium hydroxide mount and fungal cultures were negative from nail clippings. Mucosae and hair were normal. There was no lymphadenopathy or hepatosplenomegaly.

Biopsy from a hypopigmented lesion demonstrated large, pale cells with cleaved nuclei suggestive of Langerhans cells, infiltrating the papillary dermis [Figure 2a–c]. On immunohistochemistry, these cells were positive for CD1a. Epidermotropism was inconspicuous [Figure 2d]. On further probing, patient admitted having dyspnea, polydipsia and polyuria for 1 year. There was no history of smoking. Laboratory investigations of complete blood count, liver and renal function tests were normal. Positron emission tomography scan and computed tomography of chest revealed left femoral condyle infiltrates and fibrotic nodules in upper and mid zones of both the lungs respectively. Bronchoalveolar lavage showed presence of Langerhans cells in the aspirate. Plasma osmolality was increased (value: 370 mOsm/kg), whereas urine osmolality was found to be decreased (value: 145 mOsm/kg), with urine to plasma osmolality ratio being <1. Magnetic resonance imaging of brain showed absence of normal pituitary hyperintensity signal suggesting presence of central diabetes insipidus. He was started on topical corticosteroids and referred to hematology services where vasopressin nasal spray, oral prednisolone and weekly intravenous vinblastine were initiated. After 3 months, skin lesions had resolved, nails were showing improvement and polyuria and polydipsia had subsided. Treatment was continued for 6 months. Post-treatment positron emission tomography scan showed resolution of disease activity in bones. Mild fibrotic changes on computed tomography chest persisted, though there was improvement in dyspnea. Patient was still receiving vasopressin at the time of writing this report.

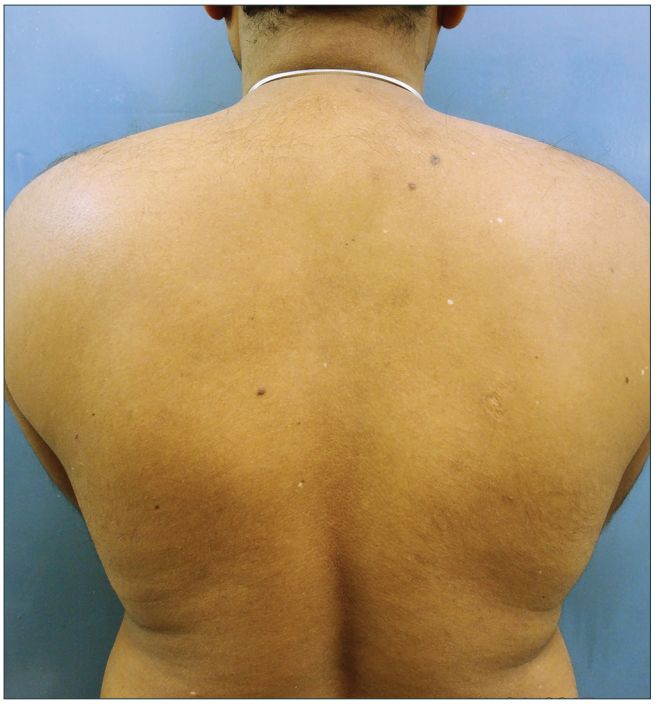

Figure 1a: Case 1: Multiple, discrete, nonscaly, hypopigmented to depigmented macules are visible on the back

Case 2: A 21-year-old man had papulopustular lesions on the face, scalp and back for 2 years. Examination revealed multiple, discrete, translucent, erythematous papulopustules of 2–3 mm size, having central umbilication and crusting, clustered on perinasal area and temporal scalp [Figure 3a]. Lower gingiva had a firm, nontender, immobile swelling of around 1 × 1 cm in size [Figure 3b]. Teeth and nails were normal. Submandibular lymph nodes were enlarged (maximum size, 3 × 2 cm), firm and non-matted. He was a nonsmoker and admitted having polydipsia and polyuria for last 6 months.

Biopsy from a facial papule revealed papillary dermal infiltration by Langerhans cells. On higher power, these cells were prominently clustered around hair follicles and stained positive for CD1a on immunohistochemistry [Figure 4a–c]. Systemic investigations revealed central diabetes insipidus, minimal pleural effusion and lytic areas in frontal skull, mandible and thoracic vertebrae. Patient was referred to hematology services and he lost to follow-up subsequently.

Langerhans cell histiocytosis is characterized by abnormal proliferation of Langerhans cells in various organ systems, and can be classified as single-system (unifocal or multifocal) or multisystem disease. Adult-onset Langerhans cell histiocytosis, though less well studied than its pediatric counterpart, can have variable presentations. Rapidly progressive form seen commonly in infants and children is less commonly observed in adults.[3,5] Moreover, pulmonary involvement is distinctly more common in adult-onset disease and has significant association with smoking. In a large retrospective study, Arico and colleagues evaluated 274 patients with adult-onset Langerhans cell histiocytosis. In single-system disease, skin was the third most common organ of involvement constituting 7.01% cases, after lungs (51.1%) and bone (38.8%). In multisystem disease, skin was involved in 50.5% cases (third most commonly involved organ) after bone (66%) and lungs (61.7%).[6]

Diabetes insipidus was diagnosed in both of our patients and is a peculiar manifestation of Langerhans cell histiocytosis. Arico *et al.* observed it in 29.6% of the patients in their retrospective review.[6] The frequency of this irreversible sequela is almost similar in adults and children. Diabetes insipidus does not respond to routine Langerhans cell histiocytosis directed treatment and requires life-long vasopressin treatment.[6]

Langerhans cell histiocytosis is a rare, but potential mimicker of common dermatoses such as seborrheic dermatitis, folliculitis, acne and intertrigo. Therefore, cutaneous manifestations, though common at the time of presentation, are easily misdiagnosed or overlooked.[3]

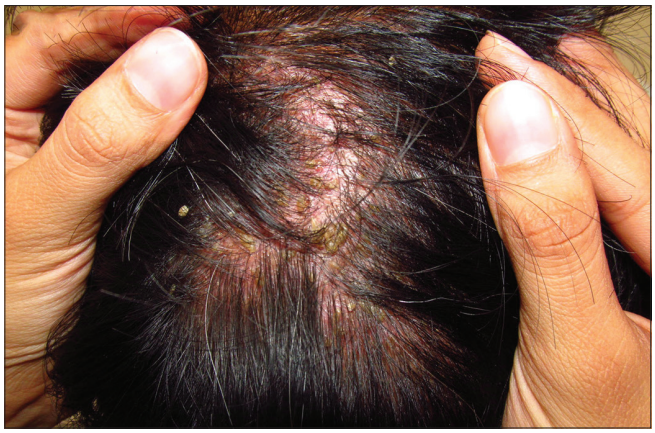

Figure 1b: Case 1: Scalp shows yellowish crusting on background erythema

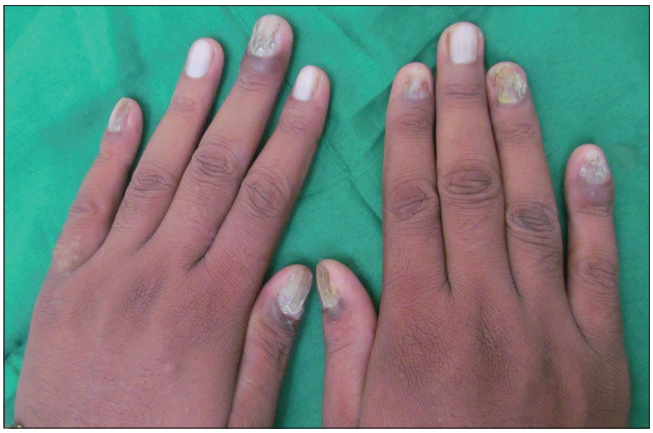

Figure 1c: Case 1: Several fingernails are showing thickening, discoloration, paronychia and onychorrhexis

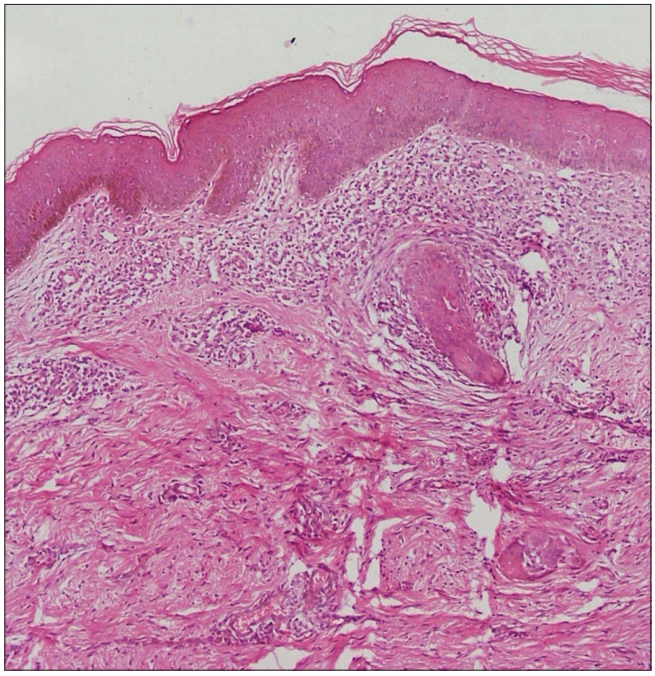

Figure 2a: Case 1: The epidermis shows mild acanthosis. Papillary dermis shows diffuse inflammatory infiltrate [hematoxylin and eosin (H and E), ×100]

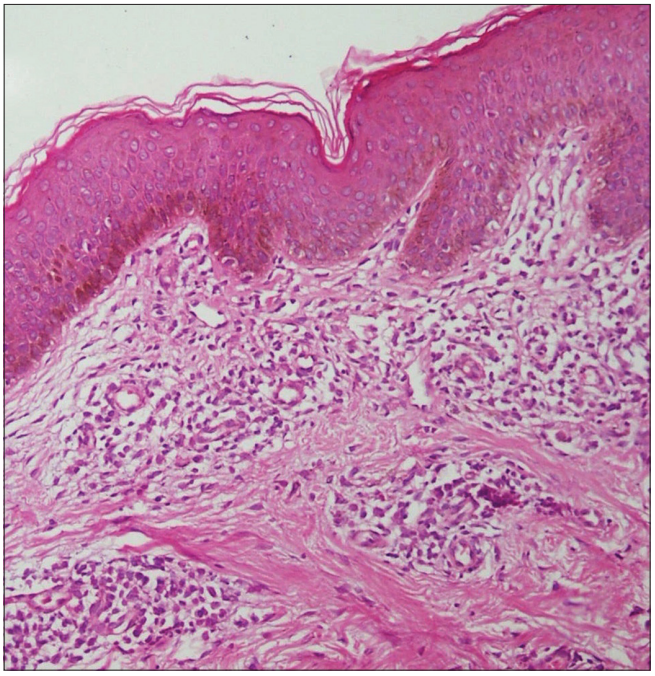

Figure 2b: Case 1: Infiltrate is composed of monomorphic cells forming clusters (H and E, ×200)

Moreover, multisystem Langerhans cell histiocytosis can present with both diffuse or localized skin involvement.[4,7] Nail involvement is considered a marker of multisystem involvement and can present as paronychia, splitting and nail loss.[8] Though our patient did not give consent for nail biopsy, no response with antifungals, a negative fungal culture and appreciable response to systemic treatment supports the diagnosis of Langerhans cell histiocytosis in nails of the first patient.

Neoplastic Langerhans cells are predominantly present in papillary dermis and have a tendency to infiltrate epidermis, and rarely extend to reticular dermis.[9] However, none of our patients showed significant epidermotropism. Perinasal facial papules and predominant perifollicular infiltrate observed in histopathology of the second patient are similar to prior observations made in adult Langerhans cell histiocytosis that showed a clinical predilection for appendage-rich sites and a periappendageal affinity of the infiltrate on histopathology.[10,11]

Clinical differential diagnoses considered for our patients were acne vulgaris, folliculitis and acne agminata for facial lesions and idiopathic guttate hypomelanosis and punctate/confetti-like vitiligo for depigmented lesions on trunk. But histopathology and immunohistochemistry clinched the accurate diagnosis.

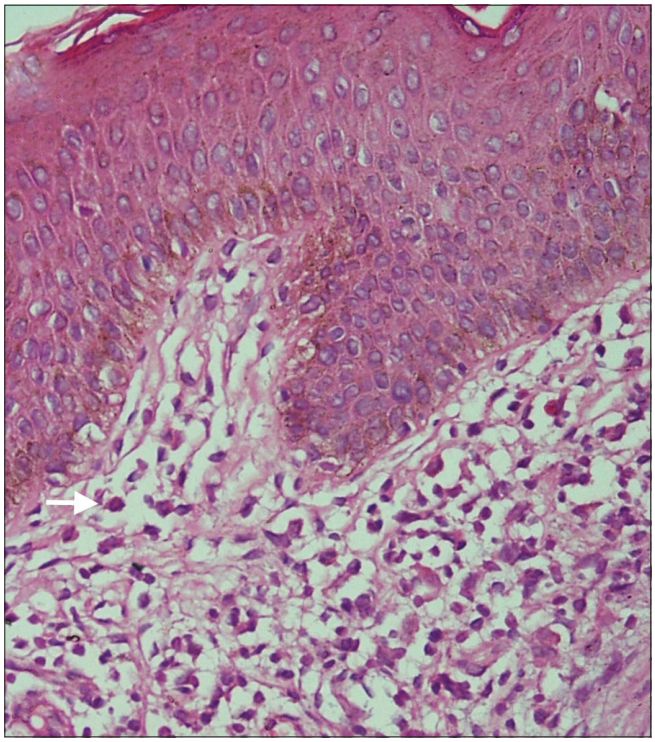

Figure 2c: Case 1: Langerhans cells with moderately abundant eosinophilic cytoplasm and indented coffee bean-shaped folded vesicular nuclei are seen admixed with histiocytes, lymphocytes and few eosinophils in the upper dermis and surrounding vessels (H and E, ×400, white arrow marks the langerhans cells)

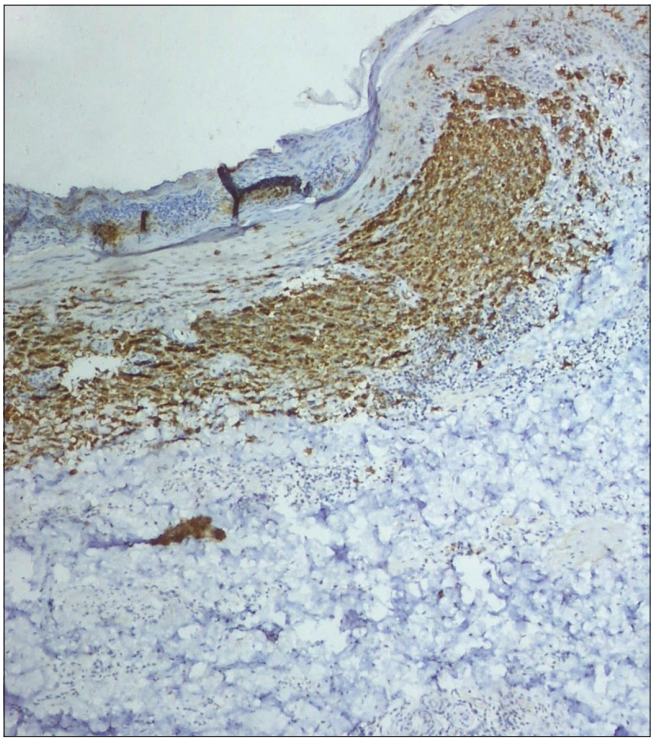

Figure 2d: Case 1: Langerhans cells staining with Cd1a (CD1a, ×100)

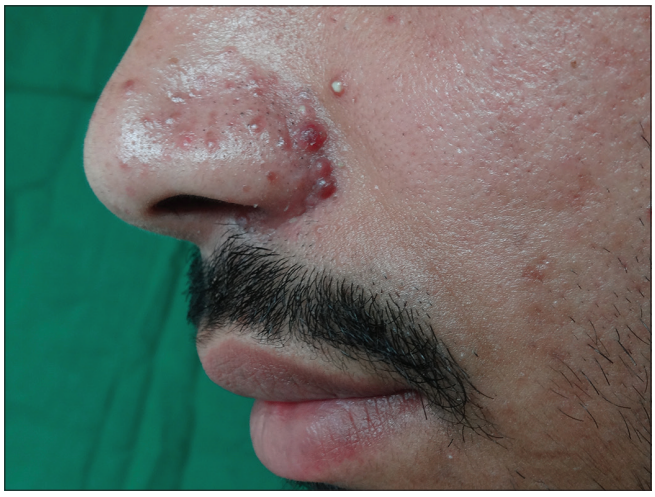

Figure 3a: Case 2: Erythematous to brownish, dome-shaped, papulopustules showing central umbilication and crusting, clustered in perinasal area

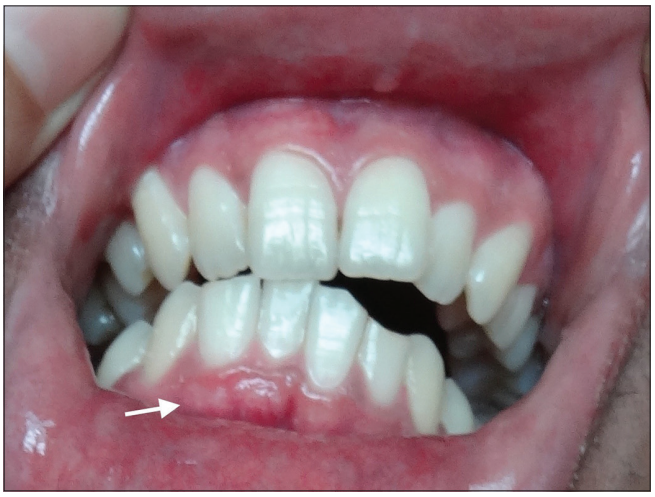

Figure 3b: Case 2: A firm, nontender, immobile swelling of around 1 cm × 1 cm in size is visible on lower gingival margin

Because of relative ease of obtaining skin biopsy, we emphasize on having a high degree of clinical suspicion for Langerhans cell histiocytosis and low threshold for skin biopsy in adults having recalcitrant acneiform lesions on centrofacial area and systemic symptoms. We also describe a novel cutaneous manifestation of adult-onset Langerhans cell histiocytosis in the form of hypopigmented/depigmented macules, which have been rarely described even in pediatric age group. [12-14]

Declaration of patient consent

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

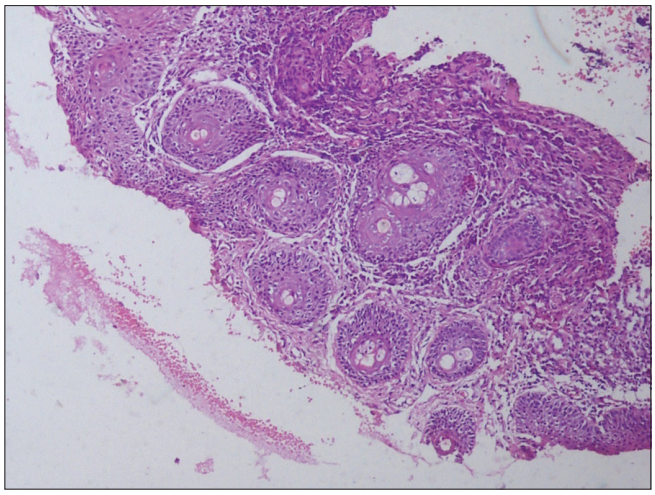

Figure 4a: Case 2: Lymphomononuclear infiltrate is visible in papillary dermis, which is clustered around follicles (H and E, ×200)

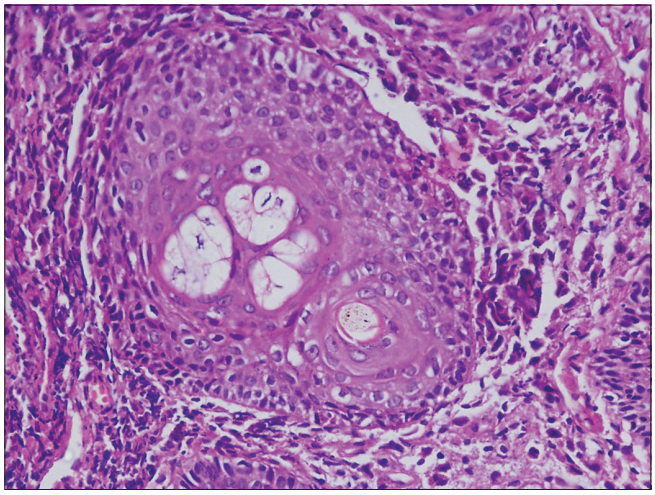

Figure 4b: Case 2: On higher power, Langerhans cells with abundant eosinophilic cytoplasm and reniform nuclei are seen admixed with histiocytes and lymphocytes (H and E, ×400)

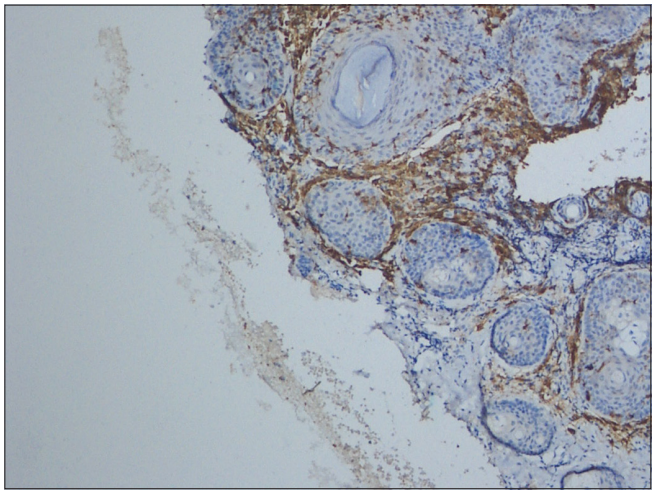

Figure 4c: Case 2: Perifollicular Langerhans cells in clusters stain positive for CD1a on immunohistochemistry (CD1a, ×200)

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Conflicts of interest
There are no conflicts of interest.

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