

Recurrent ulcers in the flexures of a 48-year-old woman

A 48-year-old woman presented with a 4-year history of recurrent painful erythematous ulcerated lesions in with purulent secretion along with fibrosis and adhesions in her right axilla [Figure 1a] and multiple severe ulcers in both groins disabling the mobility of limbs [Figure 1b]. The remainder of the mucocutaneous examination including hair, nails, teeth and mucosae was normal.

There were no constitutional symptoms. The patient had diabetes mellitus and hypertension. Systemic examination was normal. Serum biochemistry, lung function tests and, urine osmolality were all within normal limits. Bone marrow biopsy report showed no abnormality. Imaging studies were

normal. A skin biopsy specimen was obtained from the lesions.

Histopathological examination revealed a nodular infiltrated lesion in dermis. The overlying epidermis was ulcerated and the dermis showed a lesion composed of ovoid cells with moderate amounts of eosinophilic cytoplasm and an indented reniform nucleus with an admixed cellular inflammatory infiltrate of neutrophils, eosinophils and mast cells [Figure 2a and b]. On immunohistochemical study, the tumoral cells showed strong cytoplasmic positivity for CD1a and were negative for CD 68 [Figure 3].

WHAT IS YOUR DIAGNOSIS?



Figure 1: (a) Erythematous ulcers with adhesions in the right axilla. (b) Multiple severe ulcers in both groins

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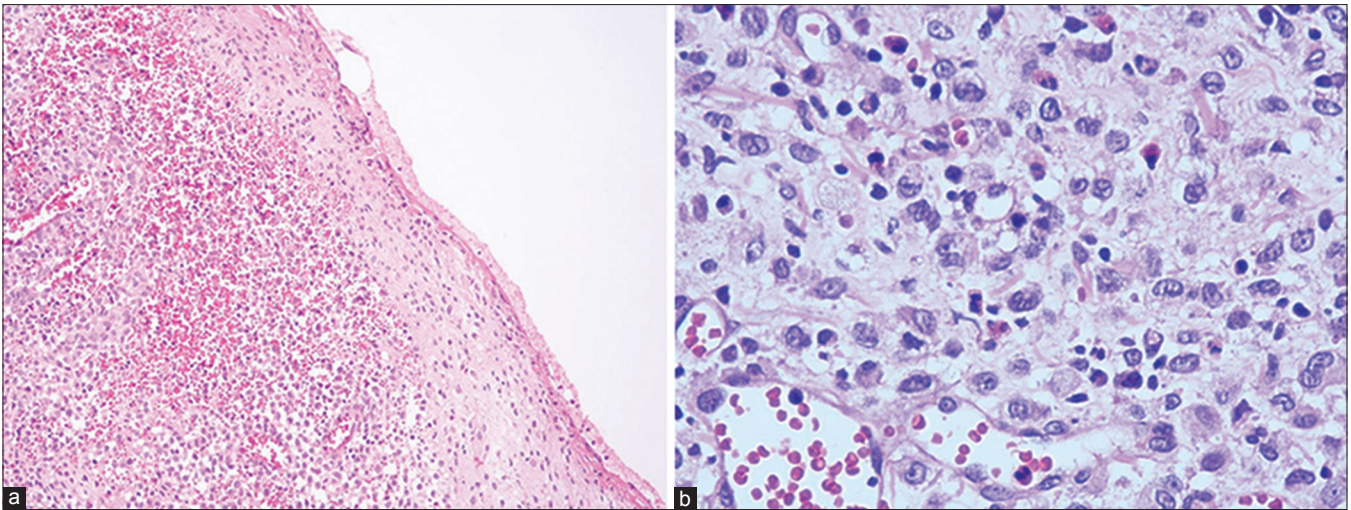


Figure 2: (a) Nodular infiltrated lesion in dermis with ulcerated overlying epidermis (H and E, $\times 10$). (b) Ovoid cells with moderate amounts of eosinophilic cytoplasm and an indented reniform nucleus with an admixed cellular inflammatory infiltrate of neutrophils, eosinophils and mast cells (H and E, $\times 400$)

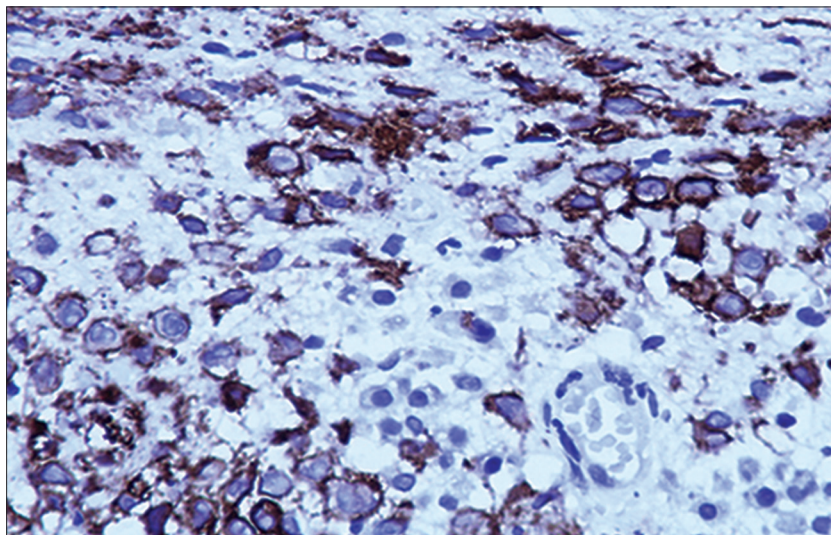


Figure 3: Immunohistochemical staining is positive for CD1a (immunostain CD1a, $\times 100$)



Figure 4: Follow-up after 6 months of thalidomide therapy showing healed lesions

ANSWER

Adult Langerhans cell histiocytosis with isolated skin involvement.

DISCUSSION

Langerhans cell was first described by Paul Langerhans in 1868. Langerhans cell histiocytosis is a rare clonal dendritic disorder of proliferating Langerhans' cells. Its incidence is 1 in 200,000 and is rarely seen in adults.^[1] Men are more affected than women and it tends to be more aggressive in women.^[2] The etiology remains poorly understood and there is controversy over whether it is a neoplastic or reactive disorder. Langerhans cell proliferation may involve one or many body systems or tissues such as bone, lung, hypothalamus/posterior pituitary gland, skin/mucous membranes, lymph nodes, liver and various soft tissues, including the testes.

Adult onset Langerhans cell histiocytosis with the sole involvement of the skin is uncommon. Clinically, it may resemble eczema, Hailey-Hailey disease, chancroid, granuloma inguinale, lymphogranuloma venereum, syphilitic chancre, tuberculosis, herpes genitalis or Behcet's syndrome.^[1] The association of Langerhans cell histiocytosis with malignant conditions such as leukaemia, myelodysplastic syndrome, Hodgkin's disease and solid tumors has been seen in greater frequency in adult onset Langerhans cell histiocytosis.^[3]

The diagnosis of Langerhans cell histiocytosis is established by skin biopsy. Histopathology shows mononuclear cells with indented reniform nuclei sharing the morphology of dendritic antigen presenting Langerhans cells along with concomitant infiltration by lymphocytes and eosinophils which may form pseudo-abscesses.^[1] Definitive histopathological diagnosis of Langerhans cell histiocytosis requires immunohistochemistry. Langerhans cell histiocytosis cells show positive immunostaining for CD1a, Langerin (CD207) and S100 and negative staining for CD68 and factor XIIIa.^[1] Electron microscopy demonstrates pathognomonic Birbeck granules, racquet-shaped cytoplasmic structures, in approximately 50% of Langerhans cells.^[1,4]

Imaging studies including skull, skeletal and chest X-ray and computed tomography scan of brain, chest, abdomen and ultrasonography of abdomen and laboratory tests such as full blood count, liver function

tests, lipid profile, serum electrolytes and coagulation studies are usually requested in the case of Langerhans' cell histiocytosis. Urine osmolality test is mandatory for assessing the presence of diabetes insipidus. All these tests were normal in our patient. More specific tests are required depending on the site and system of the suspected lesion.

The ideal therapy for Langerhans cell histiocytosis has not yet been established and varies between conservative approaches and cytotoxic or immunomodulatory drugs.^[5] The treatment options include observation, curettage, excision, intralesional corticosteroids, nitrogen mustard, external beam radiotherapy, systemic chemotherapy, immunomodulation and stem cell transplantation, all of which have been used for the management of muco-cutaneous Langerhans' cell histiocytosis with varying outcomes. Glucocorticoids have been used either topically for skin lesions or systemically for more invasive disease. When there is disseminated multi-system involvement, chemotherapeutic agents are indicated.

FOLLOW-UP

Our patient has been on regular follow-up for over 6 months. After diagnosis, we treated her with thalidomide, 100 mg in two divided doses after clinical examination for any neurological involvement and routine laboratory tests. Two months after starting thalidomide, partial improvement was noted. Complete resolution of cutaneous lesions was noted after 6 months of treatment [Figure 4] and later on, she was kept on maintenance treatment with 50 mg daily with no neurological side effects noted. Thalidomide monotherapy represents an effective, safe and well-tolerated treatment option that should be considered for single system Langerhans cell histiocytosis limited to skin, which is rare and difficult to treat.

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Conflicts of interest

There are no conflicts of interest.

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