

Solitary asymptomatic nodule on the leg

A 58-year-old man presented with an asymptomatic skin nodule on the left leg for several months. Physical examination showed a well-defined, erythematous nodule (2 cm × 1.5 cm) with a lobulated surface [Figure 1]. Differential diagnoses of squamous cell carcinoma, basal cell carcinoma and cutaneous lymphoma were considered. An excisional biopsy was performed. Histopathology showed pseudoepitheliomatous hyperplasia [Figure 2]. There was a dense, irregular, lymphoid infiltrate with admixture of neutrophils, eosinophils and large, atypical Reed-Sternberg-like cells in the dermis [Figure 3]. Immunohistochemical

analysis revealed strong positivity for CD30 [Figure 4a]. Tumor cells were also positive for the cytotoxic marker T-cell intracellular antigen-1 [Figure 4b], CD3, CD7 and CD4 [Figure 4c]. On the other hand, AE1-AE3, CD8, CD56, CD20, ALK-1, CD5, CD15 and CD25 were all negative. Routine investigations and positron emission tomography-computed tomography study were normal. There was no recurrence after 1 year of follow-up.

WHAT IS YOUR DIAGNOSIS?

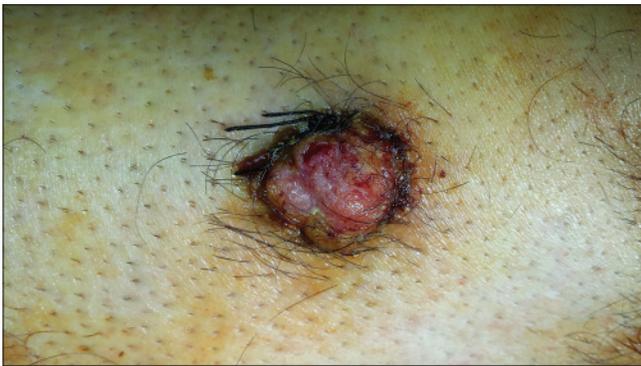


Figure 1: Asymptomatic nodule on leg

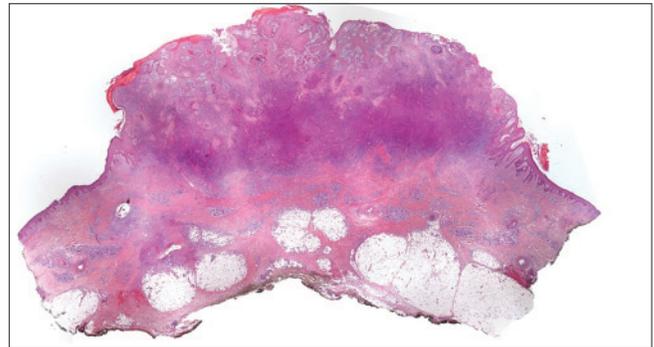


Figure 2: Pseudoepitheliomatous epidermal hyperplasia (H and E, x10)

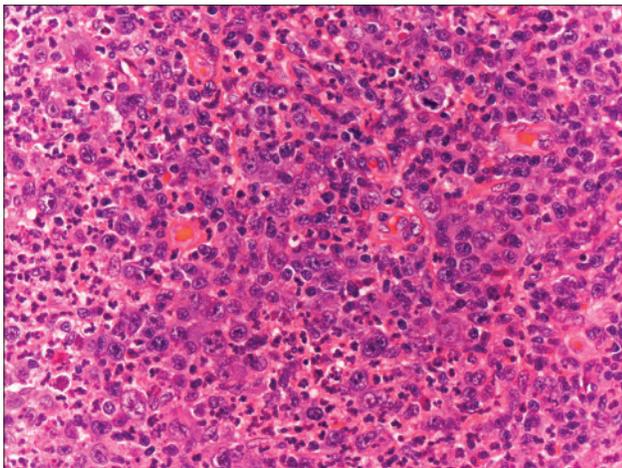
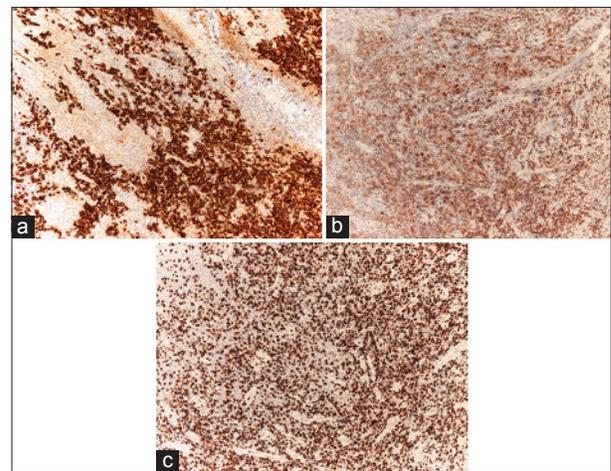


Figure 3: Dense infiltrates of atypical lymphocytes in dermis; large and atypical Reed-Sternberg-like cells (H and E, x200)



Figures 4: Neoplastic cells positive for (a) CD30 (x100), (b) cytotoxic marker T-cell intracellular antigen-1 (x100) and (c) CD4 (x100)

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ANSWER

Primary cutaneous CD30+ T-cell lymphoproliferative disorder, borderline.

DISCUSSION

Primary cutaneous CD30+ T-cells lymphoproliferative disorders are the second most common group of cutaneous T-cell lymphomas after mycosis fungoides.^[1] There are three recognized types (World Health Organization classification, 2008): primary cutaneous anaplastic large cell lymphoma, lymphomatoid papulosis and borderline lesions.^[2-4] These entities seem to represent a spectrum of related conditions that show overlapping clinical and histopathological features and may co-exist in an individual patient.^[3]

Lymphomatoid papulosis is characterized by recurrent, widespread papulo-nodular skin lesions that spontaneously regress within weeks. There are three histopathological subtypes of lymphomatoid papulosis: type A with immunoblasts, occasional Reed–Sternberg-like cells, numerous inflammatory cells, and frequent mitoses; type B with cerebriform cells, scanty inflammatory cells, and mitoses; and type C, with immunoblasts, sometimes a spectrum of cerebriform cells, a few to moderate inflammatory cells and frequent mitoses. This histopathological subtyping is of importance in the context of tumor regression; type A regresses by 4-6 weeks, type B by 8 weeks and resolution of type C is often slow and incomplete.^[5]

Primary cutaneous anaplastic large cell lymphoma presents with solitary or localized nodules often with ulceration. Partial spontaneous regression may be seen in up to 25% of lesions. It is composed of large cells with an anaplastic, pleomorphic or immunoblastic cytomorphology. Follow up clinical examinations generally help to differentiate this condition from lymphomatoid papulosis.^[1,3]

The term “borderline lesions” refers to the cases with histopathological features similar to lymphomatoid papulosis, but having a clinical course similar to primary cutaneous anaplastic large cell lymphoma, or *vice versa*.^[1,4] Borderline lesions are medium-size nodules (1–2 cm) with a tendency for slow regression. Histopathology shows large atypical cells in clusters

or sheets, usually confined to the dermis. Often a spectrum of cerebriform and large Reed–Sternberg-like cells are present. Immunophenotyping is positive for CD30, CD4, leukocyte common antigen and T-cell intracellular antigen-1.^[3-5] Neoplastic cells in primary cutaneous CD30+ T-cell lymphoproliferative disorders do not express epithelial membrane antigen and anaplastic lymphoma kinase (ALK), as in our case. However, these markers are often positive in systemic anaplastic large cell lymphoma. Unlike Hodgkin and Reed–Sternberg cells in Hodgkin’s lymphoma, neoplastic cells in primary cutaneous CD30+ T-cell lymphoproliferative disorders do not express CD15 usually, as in our case.^[1]

Differential diagnoses include other CD30+ conditions involving the skin such as systemic lymphomas, mycosis fungoides and benign disorders including lymphomatoid drug reactions, arthropod bites or viral infections. Clinicopathological correlation is mandatory to establish the diagnosis so that inadequate or excessive treatment is avoided.^[4]

Available treatment modalities for primary cutaneous CD30+ T-cell lymphoproliferative disorders are not curative. Therapeutic choice is based on lesion size, extent and clinical behavior. Patients with a few lesions may be kept under observation or the individual lesion may be excised with or without radiotherapy. In patients with more disseminated disease, low-dose methotrexate or ultraviolet light treatment may be effective.^[1,4] These disorders have an excellent prognosis with a 10-year survival rate greater than 91% for localized and 50% for generalized disease.

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Conflicts of interest

There are no conflicts of interest.

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