A rare case of CD 30 positive primary cutaneous anaplastic large cell lymphoma – masquerading as cutaneous leishmaniasis

R L Abeynayaka[1], **E M N T Nawarathna**[2], **C Gunasekera**[3], **S R Constantine**[4]

Sri Lanka Journal of Dermatology, 2019/2020, **21**: 71-73

Abstract

Primary Cutaneous CD30 positive Anaplastic Large Cell Lymphoma (C-ALCL) is a non-Hodgkin lymphoma of cutaneous origin. It accounts for 12% of all cutaneous T cell lymphomas. The clinical manifestations of anaplastic large cell lymphoma can have various presentations. We describe a 24 years old man who presented with hypopigmented skin plaques with follicular prominence over anterior and posterior trunk for two years duration and erythematous skin nodules of face and right arm for eight months duration, showing histological features of CD30 positive Anaplastic Large Cell Lymphoma after repeated skin biopsies suggestive of cutaneous leishmaniasis.

Introduction

Primary Cutaneous CD30 positive Anaplastic Large Cell Lymphoma (C-ALCL) is a non-Hodgkin lymphoma of cutaneous origin, accounting for 12% of all cutaneous T cell lymphomas. It is composed of large, anaplastic, pleomorphic T cells with expression of CD30 antigen in more than 75% of tumour cells. Most patients present with solitary or localized nodules, tumours, papules and plaques. But 20% of patients can have multiple lesions. It often ulcerates. Extracutaneous dissemination only occurs in 10% of patients. Prognosis is good. Ten years' disease related survival is 85%.

The diagnosis of cutaneous lymphoma is difficult and often delayed because of varied presentations and large number of differential diagnoses involving the entire spectrum of primary or secondary CD 30^+ lymphoproliferative diseases. The diagnosis may be difficult, particularly in early phases due to non-specific histologic findings.

Histologically these lesions show diffuse non-epidermotrophic infiltration composed of large T lymphocytes with characteristic morphology of anaplastic cells with round/oval irregular nuclei, prominent eosinophilic nucleoli and abundant cytoplasm. Neoplastic cells often express $CD4^+$, $CD30^+$. But do not express Epithelial Membrane Antigen (EMA) or Anaplastic Lymphoma Kinase (ALK).

Therapeutic methods used for these patients are generally limited. Traditional chemotherapy, surgical therapy and radiotherapy are used alone or in combination.

Case report

A 24 year old male presented with an asymptomatic, hypopigmented skin lesions over trunk (Figure 2) for two years and erythematous skin nodules over right arm and face (Figure 1) of eight months duration for which he had been prescribed numerous skin applications with poor response. Skin biopsies had never been carried out. He was free of systemic symptoms such as loss of appetite and weight, nocturnal fever or bone pain. His past medical and surgical histories were unremarkable. He is from leishmaniasis endemic area.

Examination revealed hypopigmented skin plaques with follicular prominence over anterior and posterior trunk and multiple erythematous ulcerated nodules over right arm and face. Rest of the clinical examination was normal.

The results of routine laboratory investigations were normal. The Mantoux test was negative. Bone marrow aspiration and trephine biopsy revealed no abnormality. Lymph node biopsy and radiological investigations were normal.

Keeping the differential diagnoses of mycosis fungoides transforming to tumour stage, leprosy, sarcoidosis and diffuse cutaneous leishmaniasis in mind, punch biopsy was performed which revealed diffuse infiltration of plasma cells, lymphocytes, neutrophils and histiocytes with Leishmania Donovan bodies with positive geimsa stain. Initial immunohistochemistry revealed variable positivity

[1]*Senior Registrar in Dermatology,* [2]*Registrar in Dermatology,* [3]*Consultant Dermatologist,* [4]*Consultant Histopathologist, National Hospital of Sri Lanka.*

of CD3, CD4, CD8 and CD20. Slit skin smears for leishmaniasis and leprosy were negative. Repeated punch biopsies from multiple sites were varyingly reported as non-specific and possible leishmaniasis. Skin biopsies for leishmaniasis PCR, leishmaniasis culture, TB PCR, TB culture were negative.

With high suspicion for cutaneous malignancy, deep incisional biopsy was undertaken from the ulcerated nodule of the elbow, which showed epidermal acanthosis, dermal infiltration of atypical, medium and large lymphocytes without epidermotrophism (Figure 1). The large cells had enlarged irregular nuclei with moderate cytoplasm and atypical mitosis (Figure 2). An ancillary immunohistochemistry profile revealed more than 75% positivity of atypical cells for CD30 (Figure 4) and CD3 (Figure 3). EMA also positive in proportion of large cells. MUM 1 positive in majority of large neoplastic cells.

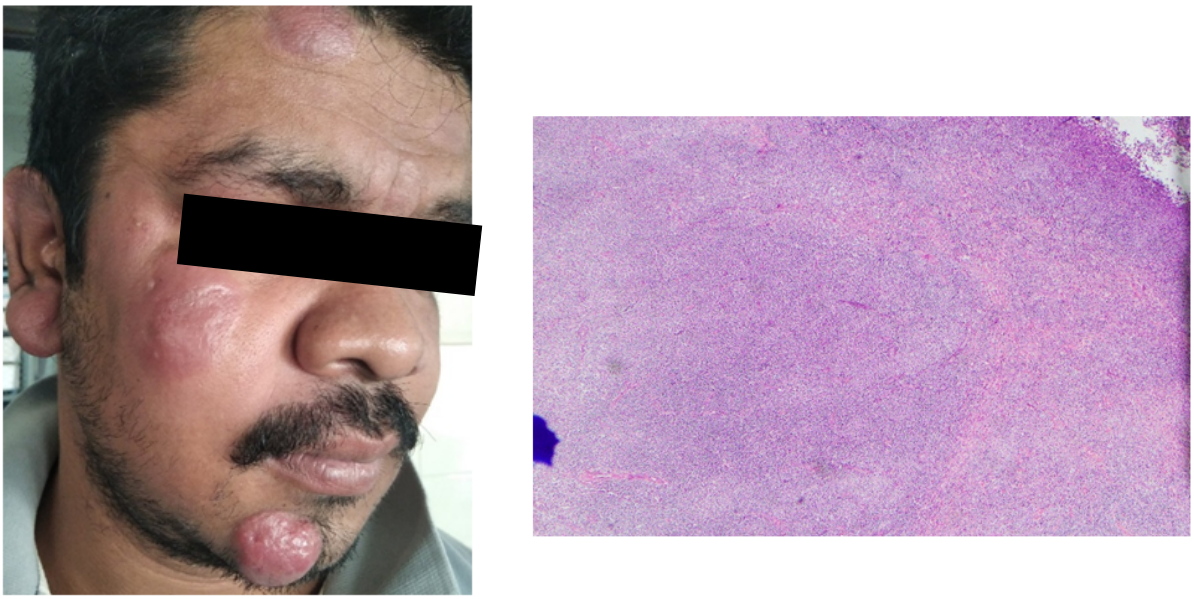

Figure 1.

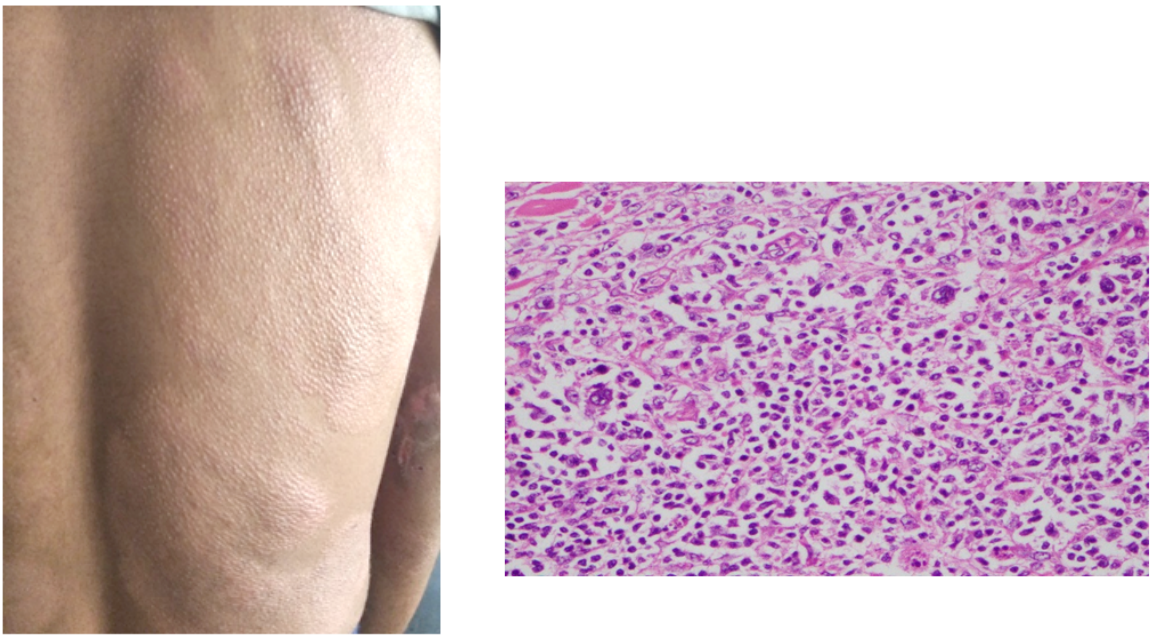

Figure 2

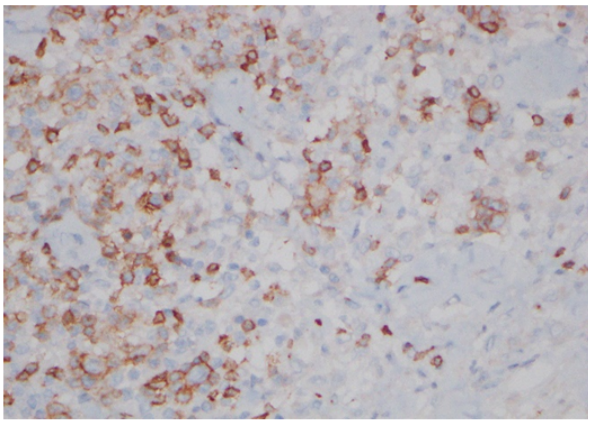

Figure 3.

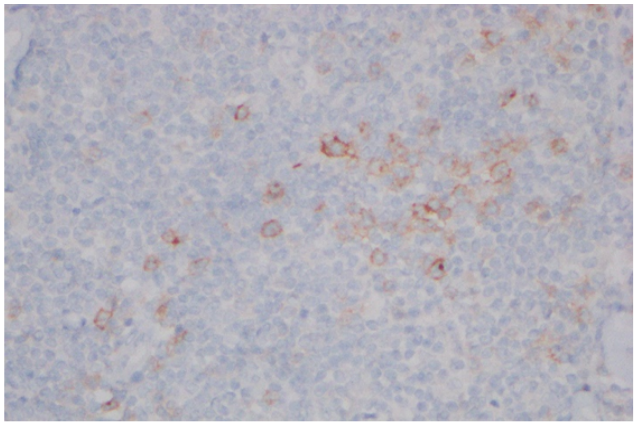

Figure 4.

Discussion

Primary Cutaneous CD30 positive Anaplastic Large Cell Lymphoma (C-ALCL) is a neoplasm composed of large atypical lymphocytes and expression of the CD 30 antigen by the majority (more than 75% of tumour cells). It is the second most common form of cutaneous T cell lymphoma with incidence of 0.1-0.2 patients per 100000.

A review of literature revealed a male predominance, adult onset (mean age 52 years). But it rarely affects children and adolescent.

Primary cutaneous CD30 positive Anaplastic Large Cell Lymphoma can be considered a mimicker, as it may resemble various other common skin diseases. In early phases of disease, the diagnosis may be difficult, with nonspecific histologic findings confounding the histopathological diagnosis.

Primary Cutaneous CD30 positive Anaplastic Large Cell Lymphoma (C-ALCL) should be differentiated from CD 30 positive lymphoproliferative disorders developing with preexisting mycosis fungoides or lymphomatoid papulosis and cutaneous involvement from primary systemic anaplastic large cell lymphoma. The differentiation relies mainly on histopathological features and immunohistochemical studies. In contrast to systemic anaplastic large cell lymphoma, cutaneous anaplastic large cell lymphoma does not express EMA, but may express the cutaneous lymphocyte antigen (CLA) and homeobox gene (HOXC5). Cutaneous Anaplastic Large Cell Lymphoma is consistently negative for the anaplastic lymphoma related tyrosine kinase (ALK).

In our patient EMA was positive in a proportion of large cells though all staging investigations are negative for systemic involvement. It was not possible to demonstrate negativity for ALK as laboratory tests were not available.

In conclusion, In all cases of nodular ulcerative lesions, cutaneous lymphoma should be considered as a differential diagnosis, and both histological and clinical suspicion are required for accurate and early diagnosis of the disease. Repeated skin biopsies and excisional biopsy of whole nodules and expanded panels of immunohistochemistry are recommended to establish the proper diagnosis.

References

1. Jean L, Bolognia, Joseph L. Jorizzo, Julie. V Schaffer. Dermatology, 4th edition.
2. Christopher EM, Griffiths, Jonathan Barker, Tanya Bleiker, Robert Chalmers, Daniel Creamer. Rook's Textbook of Dermatology, Ninth Edition.
3. James M, Amer N, *et al*. Management of multifocal primary cutaneous CD30+ anaplastic large cell lymphoma. *Journal of American Academy of Dermatology* 2004: 103-9.
4. Luciana S, Madeleyne P, *et al*. Primary cutaneous anaplastic large-cell lymphoma. *An. Bras. Dermatol.* 2013; 88.
5. Philip E. LeBoit, Gunter Burg, David Weedon, Alain Sarasin. WHO classification of Tumours – skin tumours, 2006.