

CD30-positive Anaplastic Large Cell Lymphoma of the skin in association with Mycosis fungoides: A case report

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Abstract:

CD30+ anaplastic large cell lymphoma (ALCL) can develop secondary from mycosis fungoides (MF) ; a phenomenon known as transformation of MF and is associated with aggressive clinical behaviour. However, the coexistence of MF and CD30+ALCL runs an indolent course. Further dissection of the relationship between MF and CD30+ALCL is needed. We report a case of a 73 years old Yemeni woman who presented with a four months history of an ulcerated skin lesion of the left arm. Biopsy of that lesion demonstrated light microscopic features and immunohistochemical markers of CD30+ ALCL. Further examination of the patient revealed multiple eczematous lesions of the lower extremities. Biopsy of one of those lesions revealed histology of patch stage mycosis fungoides. The cell morphology and clinical behaviour are consistent with MF and CD30+ALCL coexistence.

Case report :

In January 2003 a 73 yrs old Yemeni female was referred from dermatology clinic complaining from skin lesion on the right arm of 4 month duration, painless, gradually increase in size started as eczematous plaque then start to ulcerate, no discharge, not associated with systemic changes such as fever, weight loss, but it was associated with similar skin lesion on right thigh and left leg and a biopsy was taken from right thigh by dermatologist as a suspected case of (MF). She was in good condition and no complaint of any relevance.

On examination the patient was in fair condition, no sign of chronic illness. Locally, there was an ulcerated lesion on posterior aspect of distal end of right arm, measuring 4x5cm in diameter, rounded

in shape, ulcerated, raised edge, no discharge, non tender, no skin changes around it(Fig1), no local lymphadenopathy CBC:6.3x10/ml,hgb:11.9/dl, cholesterol:8,CXR: normal,U/S abdomen: no organomegally. C/T chest, abdomen, pelvis: no evidence of metastatic disease seen in liver or lung and no evidence of mediastinal or retroperitoneal lymphadenopathy.

Histopathology of eczematous lesion from the thigh (Figs2,3) showed slightly acanthotic epidermis with colonization of the basal cell layer by atypical CD3+CD4+ lymphoid cells, papillary dermis fibrosis and sparse superficial and perivascular lymphoid dermal infiltrate (figs2,3). Subsequent biopsy from an ulcerated tumoural mass from left elbow showed diffuse infiltration of the dermis and subcutis by sheets of atypical large lymphocytes with abundant cytoplasm, vesicular "embryo"-shaped nuclei , one or more large nucleoli and occasional multinucleated "wreath" cells. Immunohistochemical markers showed the tumour cells to be diffusely and strongly CD30+ and non B non T (null cells). The overlying epidermis was ulcerated but the ulcer edges did not show epidermotropism by neoplastic lymphocytes (figs 4,5,6).



Fig(1)Clinical appearance of patient's ulcer on posterior of distal end of right arm .

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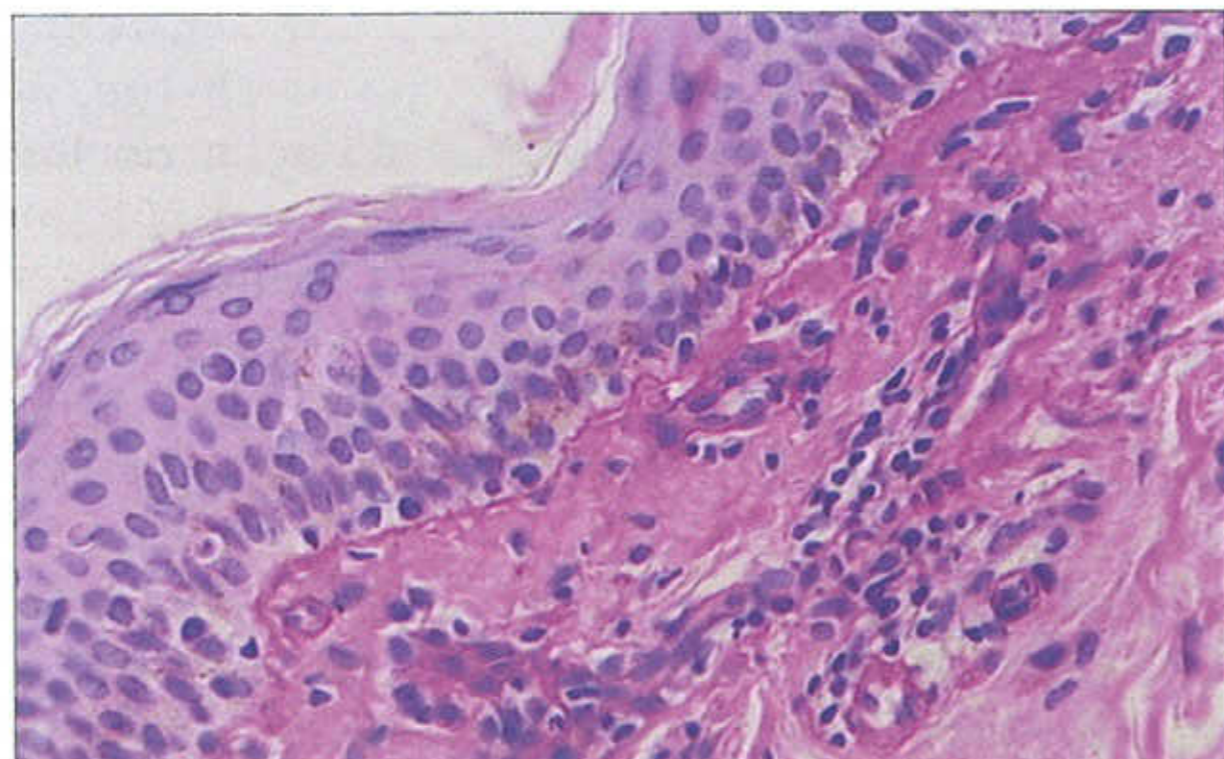


Fig (2) Light microscopy of a section from an eczematous lesion showing colonization of the basal layer of epidermis by lymphoid cells with hyperchromatic atypical nuclei and irregular nuclear contours. Note absence of anaplastic large cell lymphoma cells in the underlying dermis. (PAS stain; original magnification x 96).

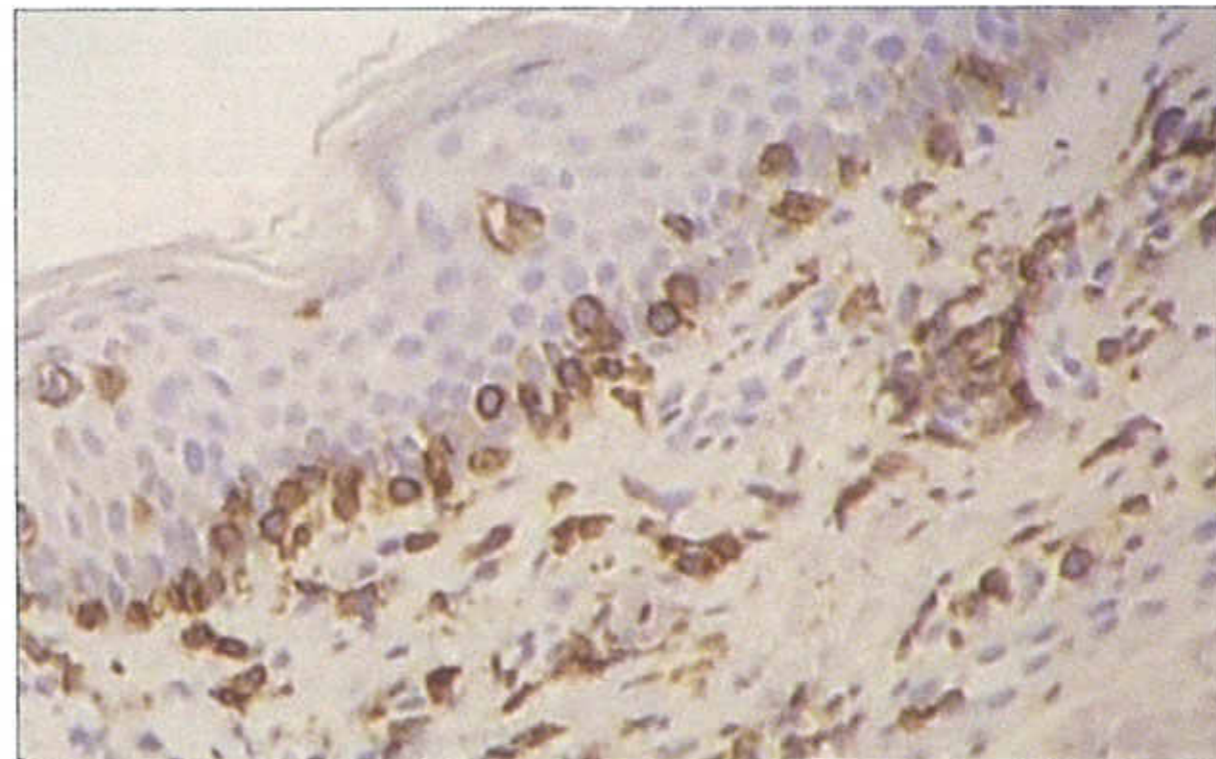


Fig (3) Immunohistochemical stain (CD4) visualising the colonization of the basal layer of epidermis by CD4+ T lymphocytes (original magnification x 96).

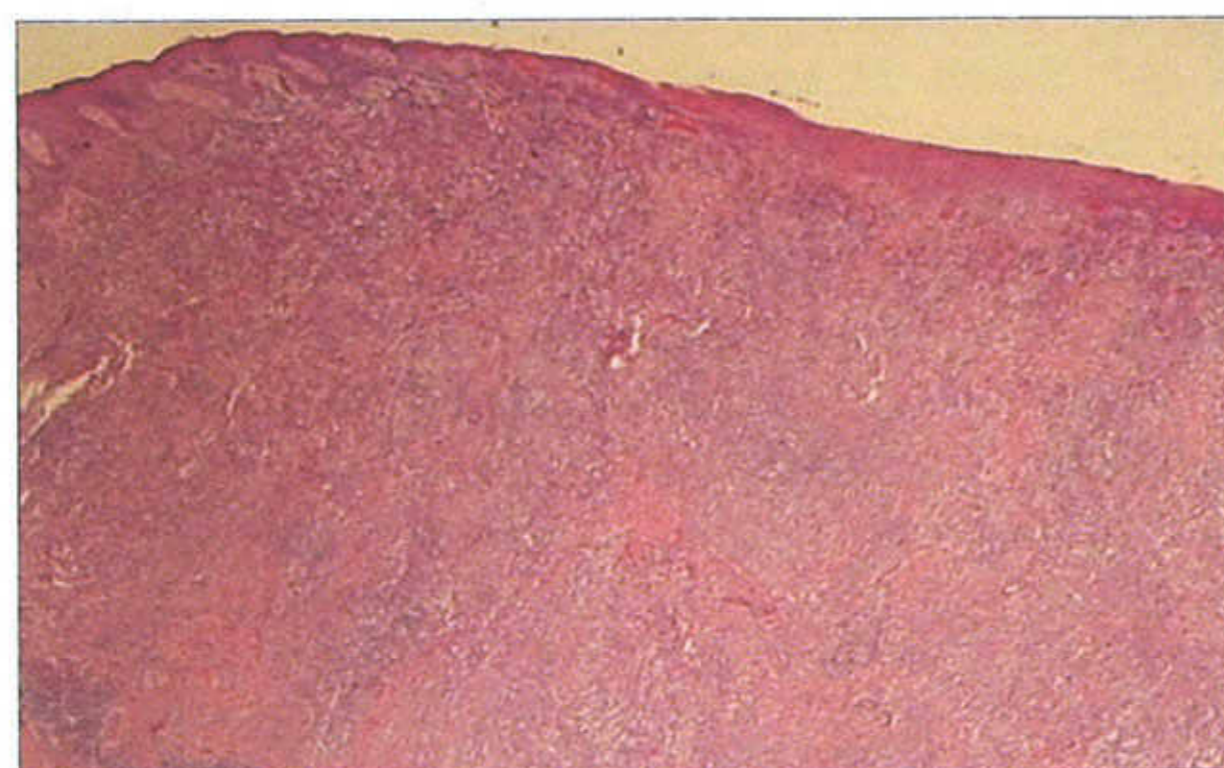


Fig (4) A panoramic view of a histologic section from a tumoural lesion showing diffuse infiltration of the dermis and subcutis by sheets of ALCL cells; note ulceration of the overlying epidermis (hematoxylin & eosin stain; original magnification x64).

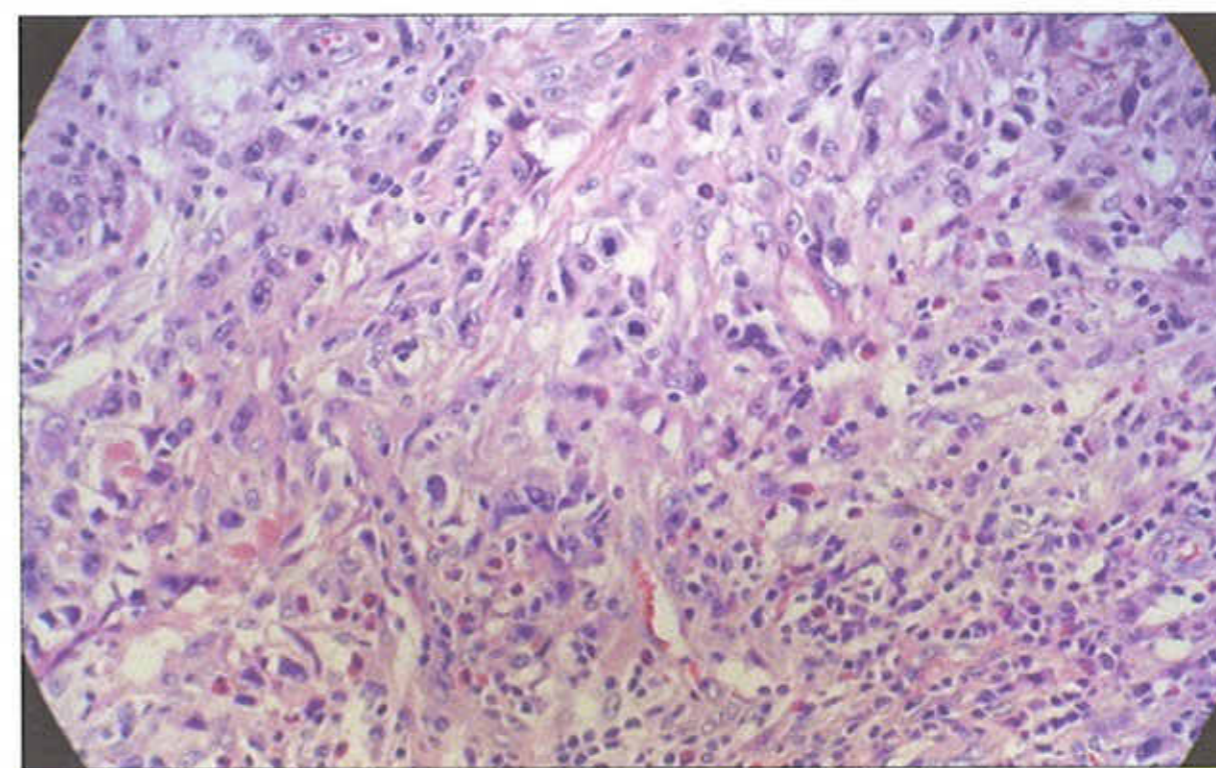
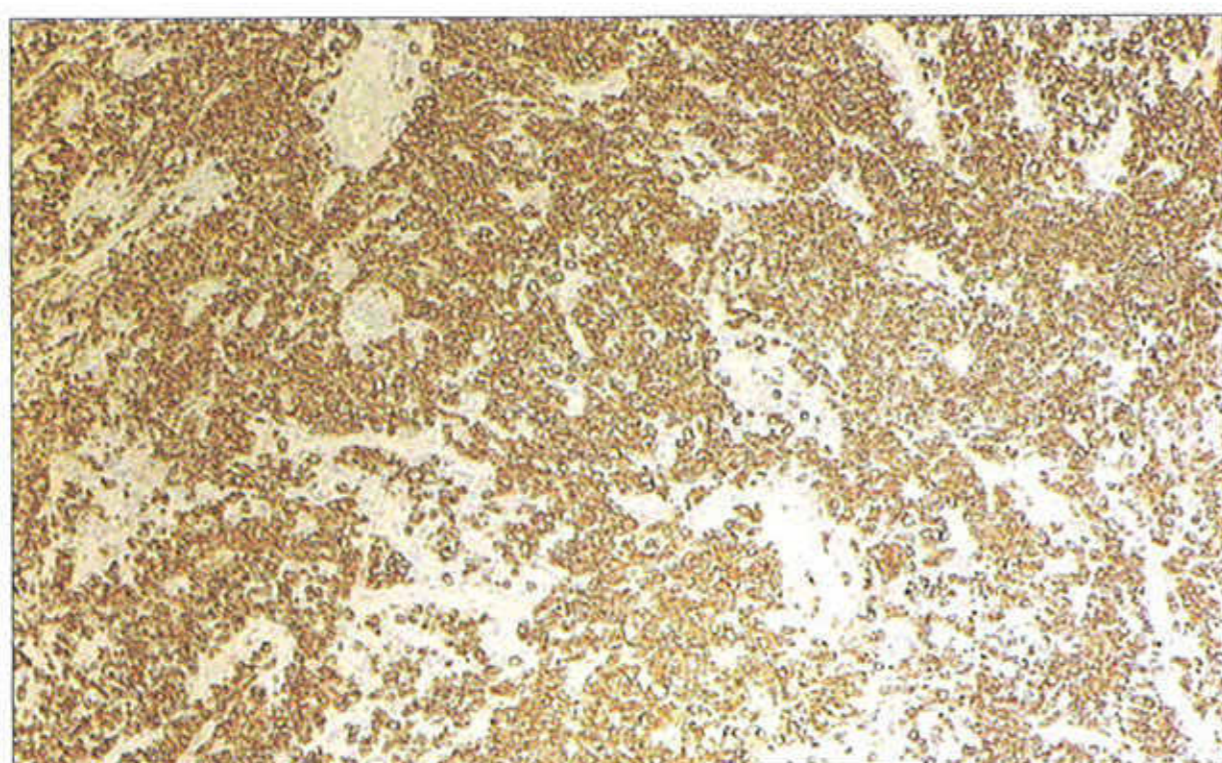


Fig (5) A higher power view of ALCL cell infiltrate of the dermis showing sheets of large lymphoid cells with atypical "emryo-shaped" vesicular nuclei and multiple prominent nucleoli (hematoxylin&eosin stain; original magnification x 140).



Fig(6)Immunohistochemical stain of CD30 marker showing diffuse CD30+ membranous staining of the ALCL cells in dermis and subcutis (original magnification x96).

Discussion :

Anaplastic large cell lymphoma (ALCL) is a common nodal disease that expresses strong reactivity with antibodies directed against CD30; a T-cell activation-associated antigen. Hence the commonly used name of CD30+ALCL⁽¹⁾. Primary ALCL arises de novo and can be subdivided into systemic (nodal) and cutaneous forms. Primary cutaneous ALCL is often indolent whereas primary nodal ALCL is a moderately aggressive tumour. Secondary cutaneous ALCL represents a morphologic and biologic transformation of another lymphoma such as mycosis fungoides (MF)⁽²⁾. Transformation of MF to CD30+ ALCL is usually associated with a more aggressive biological behaviour and rapidly fatal outcome. No significant behavioural differences between tumoural stage MF and CD30+ALCL from MF⁽³⁾. The coexistence

of patch stage MF and CD30+ALCL have been reported and unlike MF transformation their coexistence was associated with a favourable indolent clinical course⁽⁴⁾. ALCL is currently undergoing reappraisal since it has a broad spectrum of biologic characteristics and because expression of CD30 no longer defines the disease⁽⁵⁾. Studying the overlap of various forms of primary cutaneous T-cell lymphomas (CTCLs) can provide further insight into the issue of ALCL reappraisal. Further dissection of the relationship between these “smoldering” forms of CTCLs is needed.

Transformation of mycosis fungoides (MF) into biologically aggressive anaplastic large cell lymphoma (ALCL) is well documented⁽³⁾. However; the literature showed only rare reports of the coexistence of the two diseases where the indolent course of MF and ALCL is maintained^(3,7,8). Our case report presents another rare example of MF and ALCL coexisting in the same patient at the time of presentation. The two lesions were distinct clinically and histologically. The eczematous lesions showed histology of patch stage MF as shown by epidermotropism of atypical CD3+CD4+ cell population and the lack of tumoural dermal infiltrate. On the other hand the tumoural lesions showed the classical histology of ALCL with diffuse dermal infiltrate by sheets of atypical, large lymphocytes with abundant cytoplasm, vesicular “embryo”-shaped nuclei, one or more large nucleoli and occasional multinucleated “wreath” cells. Immunohistochemical markers showed the tumour cells to be diffusely and strongly CD30+ and non B non T (null cells). Clonality of tumour cells in the two lesions could not be tested as molecular genetic testing for clonal rearrangement of T cell receptor (TCR) gene was not available in our laboratory. Nonetheless our case is thought to be consistent with the coexistence of MF and

CD30+ALCL, rather than CD30+ALCL transformed form of MF.

In our review of literature we could find three previous case reports of the coexistence of MF and CD30+ALCL by Kang et al in 2000⁽⁶⁾, Lee et al in 1999⁽⁷⁾ and Woodrow et al in 1996⁽⁴⁾. The latter two case reports showed the same clonal rearrangement of TCR gene in the lesions of MF and CD30+ALCL. In the case report by Kang et al⁽⁶⁾ the clonal rearrangement of TCR was not found in the patch stage of MF.

In 1992 Cerroni et al⁽³⁾ have reported a series of 36 patients with MF associated with tumoural lesions. They found that 20 out of their 36 patients (55.6%) showed transformation to ALCL. The transformed large cells had similar clonal rearrangement of TCR suggesting that the presence of large cells within the tumoural MF infiltrate is the result of transformation of morphologic features of the cells rather than expansion of a different clone of neoplastic cells. Clonal molecular genetic similarities have also been found among cutaneous lymphomas ranging from lymphomatoid papulosis LyP to MF and ALCL⁽⁸⁾.

CD30+ALCL and LyP coexisting with MF run an indolent course; therefore the criteria of CD30+ALCL proposed by Willemze⁽⁹⁾ whether the coexistence with other diseases such as LyP and MF should be excluded or not in diagnosing cases of CD30+ALCL is debatable. Furthermore Kantor et al⁽¹⁰⁾ have demonstrated increased risk of second malignancy in patients with cutaneous T-cell lymphoma CTCL including Hodgkin’s lymphoma; other forms of non Hodgkin’s malignant lymphoma and non lymphoid malignancies including lung and colorectal cancer. Similar case reports are needed for further clarification of the relationship between various forms of CTCLs and between CTCLs and other forms of human cancer.

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