

A case of exuberant cutaneous lymphomagenesis in the setting of chronic patch mycosis fungoides

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INTRODUCTION

Patients with mycosis fungoides (MF) are at increased risk of a second malignant neoplasm, especially lymphoma.¹ We report a sexagenarian with a 14-year history of patch MF, stage IB, who had intravascular cutaneous anaplastic large cell lymphoma (ALCL) and cutaneous composite lymphoma (CL) of B-cell and T-cell origin in sequential series as late complications.

CASE REPORT

The clinical presentation of both lymphomas was similar, consisting of eruptive asymptomatic papulonodular lesions invariably associated with preexisting patch MF without adenopathy or other constitutional symptoms (Fig 1). Biopsy of the first lesion, which developed over the left suprabrow, found dilated ectatic vascular structures in the dermis and subcutis with intraluminal large, pleomorphic, mononuclear cells positive for CD3, CD4, β F1, and CD30 (Fig 2). Results of CD20, CD56, Alk-1, EMA, and Epstein-Barr virus (EBV) in situ hybridization studies were negative. Peripheral blood flow cytometry findings were unremarkable. Results of positron emission tomography/computed tomography and a bone marrow biopsy were normal. On the basis of the exclusive intraluminal location of the neoplastic cells, the anaplastic cytology, the CD30⁺/Alk-1–negative phenotype, and a negative staging workup, a diagnosis of cutaneous intravascular ALCL was rendered, and the patient was treated with systemic chemotherapy with

Abbreviations used:

ALCL: anaplastic large cell lymphoma
 CL: composite lymphoma
 EBV: Epstein-Barr virus
 MF: mycosis fungoides

cyclophosphamide, doxorubicin, vincristine, and prednisone for 6 cycles, which were completed in September 2010.

The patient remained clear except for residual patch MF until late 2013 when multiple smooth erythematous papules developed on the torso. Multiple skin biopsies found a mixed bandlike and focally nodular dermal mononuclear infiltrate comprised of immunophenotypically distinct B-cell and T-cell populations (Figs 3 and 4). In situ hybridization studies for EBV were negative. Immunoglobulin heavy chain and T-cell receptor gene rearrangement studies by polymerase chain reaction confirmed dual B-cell and T-cell clones. This T-cell clone was identical to the original T-cell clone identified a decade prior when the original diagnosis of MF was made. Repeat positron emission tomography/computed tomography staging and peripheral blood flow cytometry findings were unremarkable. Given the negative staging workup and the simultaneous presence of 2 morphologically distinct lymphomas at a single tissue site, a diagnosis of composite lymphoma comprised of MF and primary cutaneous B-cell marginal zone lymphoma was rendered. Systemic treatment was deferred given a lack of symptoms, limited skin involvement, and the indolent nature of the B-cell component.

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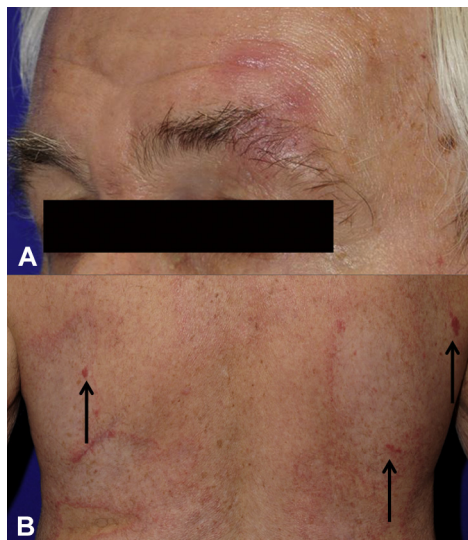


Fig 1. **A**, New-onset infiltrated arciform thin plaque over left suprabrow. **B**, Eruptive smooth papules (black arrows) admixed with chronic epidermally atrophic annular patches.

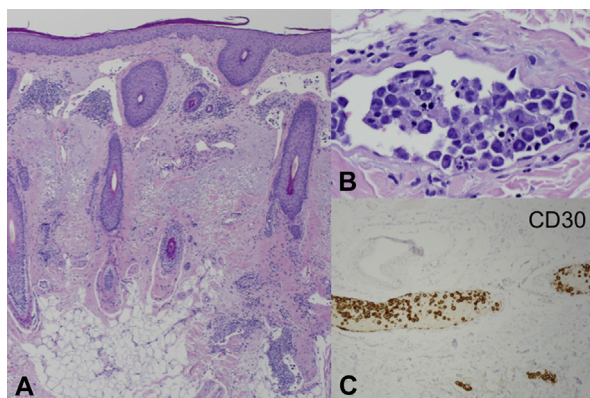


Fig 2. Dilated ectatic blood vessels in the dermis and subcutis (**A**) with intravascular pleomorphic anaplastic cells (**B**) positive for CD30 (**C**). (**A** and **B**, hematoxylin-eosin stains; original magnifications: **A**, $\times 4$; **B**, $\times 40$; **C**, original magnification: $\times 20$).

DISCUSSION

Cutaneous intravascular ALCL and cutaneous CL are very rare entities. Most composite lymphomas involving the skin have an underlying systemic B-cell component derived from chronic lymphocytic leukemia or small lymphocytic lymphoma.² Uniquely, the B-cell component in this case is cutaneous in origin with a marginal zone phenotype given an absence of bcl-6/CD23 staining and an associated T-cell-rich infiltrate.³ Although cutaneous lymphoid hyperplasia and cutaneous marginal zone lymphoma may have morphologic overlap, the presence of clonality along with an

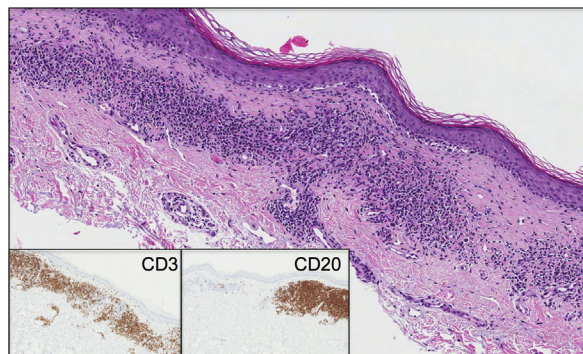


Fig 3. Shave biopsy from a chronic patch shows a bandlike and focally nodular atypical mononuclear superficial dermal infiltrate. (Hematoxylin-eosin stain, original magnification: $\times 10$). The bandlike component had positivity for CD2, CD3 (inset, original magnification: $\times 10$), and CD4. The nodular aggregates were CD20 positive (inset, original magnification: $\times 10$). The identified B-cell and T-cell populations were clonal by gene rearrangement studies.

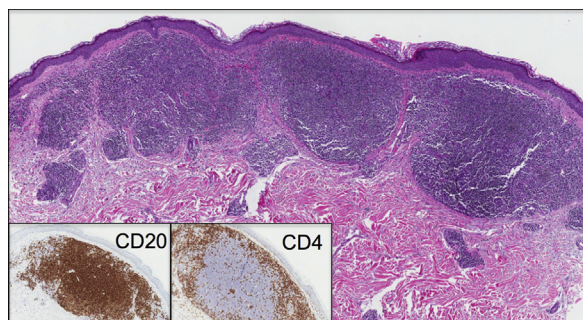


Fig 4. Punch biopsy from a new-onset papule shows nodular dermal aggregates (hematoxylin-eosin; original magnification: $\times 10$) of B cells positive for CD79a, CD20 (inset, original magnification: $\times 10$), and BCL-2 but negative for CD5, BCL-6, CD10, and CD23 consistent with cutaneous marginal zone lymphoma. These aggregates were surrounded by a T-cell infiltrate that on the lateral edges was bandlike in configuration and positive for CD3 and CD4 (inset, original magnification: $\times 10$) and negative for CD8 and CD30. Dual clonal B-cell and T-cell populations were identified by gene rearrangement studies.

absence of eosinophils, tingible foreign body macrophages, and a mixed T-cell infiltrate is most consistent with the latter.⁴ This finding represents a true cutaneous composite lymphoma and not simply a secondary B-cell lymphoma, as skin biopsies and immunohistochemical and molecular analyses demonstrate the simultaneous coexistence of 2 distinct primary cutaneous B-cell and T-cell lymphomas. The presence of dual B-cell and T-cell clones is strong evidence against the possibility of phenotypic lineage infidelity, whereby a T-cell lymphoma develops aberrant expression of B-cell

surface markers. Furthermore, this is less likely to reflect genotypic lineage infidelity, as there is morphologic evidence of a cutaneous B-cell lymphoma and T-cell lymphoma in the setting of an identical T-cell clone identified a decade prior.

With the exception of this index case, previous descriptions of intravascular cutaneous ALCL do not show a consistent association with pre-existing MF and more prototypically develop de novo as solitary or progressive papulonodular eruptions.⁵ Attempts in this case to clonally link the prior MF with the subsequent intravascular cutaneous ALCL were not successful, as there was inadequate amplification of both T-cell receptor target DNA and an internal control despite the use of laser microdissection. The clinical presentation and histopathologic features were also not consistent with large cell transformation of MF.⁶ Other benign intravascular CD30⁺ proliferations simulating intravascular lymphoma have a pyogenic granulomalike histopathology and a significant inflammatory cell component and were absent in this case.⁷

The optimal treatment of intravascular cutaneous ALCL is unknown. Systemic chemotherapy was selected in this case, as most intravascular large B-cell lymphomas and EBV⁺ natural killer/T-cell lymphomas exhibit rapid systemic dissemination. Our patient has not had a recurrence of ALCL since the end of systemic chemotherapy 4 years ago. Similar favorable long-term outcomes have been observed in other cases, suggesting that skin-limited intravascular CD30⁺ ALCL may be a distinctive clinical pathologic entity with potentially indolent behavior akin to other extravascular cutaneous CD30⁺ lymphoproliferative disorders.⁸ In this context, consideration of skin-directed therapy or low-dose oral methotrexate as initial therapy is warranted.

Patients with MF may have multiple other lymphomas that rarely may be purely cutaneous in origin. The initial clinical presentation may mimic

worsening or transformed MF; thus, early consideration should be given to biopsy of lesions discordant from prior baseline. Long-term prognosis is related the specifics of the underlying subsequent lymphoma, which, in the case of skin-limited ALCL, has yet to be completely elucidated. Treatment is largely empiric guided by presenting symptoms and disease extent in conjunction with expectant management emphasizing cutaneous or systemic progression.

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