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Secondary cutaneous involvement by systemic ALK-negative anaplastic large cell lymphoma with 6p25.3 rearrangement

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Sir: We read with interest the recent report by Onaindia et al¹ describing 3 primary cutaneous anaplastic large cell lymphomas (ALCLs) with 6p25.3 rearrangements and histological features similar to those we described in cases of lymphomatoid papulosis (LyP) bearing this rearrangement.² Here we extend these findings to include a case of secondary cutaneous involvement by systemic ALK-negative ALCL with identical histological features, 6p25.3 rearrangement, and excellent long-term outcome.

A 56-year old male presented in 1982 with inguinal adenopathy. No skin lesions were present. Lymph node biopsy on subsequent review revealed ALK-negative ALCL extensively involving the node and demonstrating a lymphohistiocytic histologic pattern as previously described.³ The patient recalled having adenopathy at other sites, though complete staging data were not available. The patient received CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone; number of cycles unknown) and achieved a complete remission. He received maintenance chemotherapy including cyclophosphamide, chlorambucil, vincristine and prednisone (doses/schedules unknown). All chemotherapy was discontinued as of 1995 with no known relapses between 1982 and 2011, when he presented with a solitary skin lesion on the right neck that showed involvement by ALK-negative ALCL. The patient was otherwise asymptomatic and a staging PET scan and bone marrow biopsy were negative. The patient received no further treatment following excision and died without evidence of disease relapse in 2013 at age 87.

The 2011 skin specimen showed an atypical lymphoid infiltrate involving the epidermis and dermis (Fig. 1). The epidermotropic component contained small lymphocytes with convoluted, hyperchromatic nuclei, whereas the dermis contained sheets of large cells including hallmark cells. The tumor cells were positive for CD2, CD3, CD4, CD30, and T-

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Conflict of interest

The authors declare no potential conflicts of interest.

cell receptor- (TCR-) β F1, with partial loss of CD5 and CD7 and negativity for TIA1, ALK, and TCR- $\gamma\delta$, similar to the original lymph node biopsy. PCR studies showed clonal TCR- β and - γ rearrangements of the same size in both specimens, suggesting a clonal relationship (Fig. 2). Fluorescence *in situ* hybridization⁴ demonstrated 6p25.3 rearrangement in both specimens.

We reported 11 cases of a distinct subtype of LyP with unique histological features, including a biphasic morphological pattern with large transformed lymphocytes in the dermis and pagetoid reticulosis-like infiltration of the epidermis of smaller atypical lymphocytes.² Staining for CD30 often was biphasic, with strong staining in the dermis and weaker staining in the epidermis. All 11 cases with these features had 6p25.3 rearrangements (also known as *DUSP22* rearrangements). The present case demonstrates that these features can be observed beyond the setting of primary cutaneous T-cell lymphoproliferative disorders, and provides further support for a relationship between the genetic and histological features as suggested by Onaindia et al.¹ Cytokine-mediated homing might contribute to the pagetoid reticulosis-like epidermotropism in these cases. For example, we recently reported that ALCLs with 6p25.3 rearrangements overexpress the skin-homing chemokine receptor gene, *CCR8*.⁵

The present case also emphasizes that presence of a 6p25.3 rearrangement does not exclude the possibility of a systemic origin for ALCL involving the skin. Regardless of genetics, patients with ALCLs involving the skin require careful clinical evaluation and staging to ensure they receive appropriate therapy. In a recent study on the genetics of systemic ALK-negative ALCL, we found 6p25.3 rearrangements in 30% of cases.⁶ These cases had favorable overall survival rates similar to those observed in systemic ALK-positive ALCL, as exemplified by the present case.

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Figure 1.

Secondary cutaneous involvement by systemic ALK-negative ALCL with 6p25.3 rearrangement. A. Low-power photomicrograph of skin lesion. B. Epidermotropic infiltrate of small lymphocytes. C. Sheet-like growth of large cells including “hallmark” cells (inset). D. Epidermotropic component staining for CD3. E. Dermal component staining for CD3. F. Epidermotropic component staining weakly for CD30. G. Epidermotropic component staining strongly for CD30.

Figure 2.

Comparative molecular findings in presenting lymph node (1982) and secondary cutaneous involvement (2011). A. Capillary electrophoresis tracings demonstrating clonal peaks for T-cell receptor-β from lymph node. B. Tracings demonstrating identical peaks in subsequent skin biopsy. C. FISH image from lymph node biopsy using breakapart probe showing one intact fusion signal (*f*) and one split signal (arrows), indicating a 6p25.3 rearrangement. D. FISH image from subsequent skin biopsy, showing same features.