DOI: 10.3315/jdcr.2008.1013

Journal of Dermatological Case Reports

Primary cutaneous CD30+ anaplastic large cell lymphoma: report of a rare case

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Key words:

primary cutaneous anaplastic large cell lymphoma, primary cutaneous CD30 positive large T cell lymphoma, lymphoproliferative disorders, mycosis fungoides, lymphomatoid papulosis

Abstract

Primary cutaneous anaplastic large cell lymphoma (PCALCL) is a rare type of non-Hodgkin's lymphoma comprising approximately 0.9-9.0% of all cutaneous lymphomas. PCALCL is characterized by the absence of systemic involvement, spontaneous regression and low recurrence rate especially in localized lesions.

We present a 47-year-old female with a 1½-year history of two asymptomatic erythematous indurated plaques on the right arm. Skin punch biopsy revealed dense infiltrates of non-epidermotropic, large, irregularly-shaped lymphocytes with hyperchromatic and pyknotic nuclei. Immunohistochemistry revealed that these atypical cells are anaplastic lymphoma kinase (ALK) positive, CD30+, CD3-, CD20- and epithelial membrane antigen (EMA) negative. Clinical, histopathological and immunohistochemical findings are consistent with PCALCL. Work-ups revealed no systemic involvement. Short course CHOP (Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) chemotherapy resulted in total resolution of skin lesions; however, recurrence was noted 12 months after treatment. She then underwent radiotherapy and achieved complete remission.

Because the clinical presentation of PCALCL can be variable, a high index of suspicion is necessary in patients presenting with chronic plaques and nodules unresponsive to topical or oral medications.

Introduction

Primary cutaneous lymphomas are cutaneous T- or B-cell lymphomas that present in the skin with no evidence of extracutaneous disease at the time of diagnosis.[1,2] Primary cutaneous CD30+ lymphoproliferative disorders, accounts for 30% of the primary cutaneous T-cell lymphomas (CTCL) and includes the following: primary cutaneous anaplastic large cell lymphoma (PCALCL), lymphomatoid papulosis (LyP) and borderline cases.[1,3]

PCALCL has variable clinicopathologic and immunologic features thus making it a mimic of several skin diseases. It is characterized by the absence of systemic involvement at presentation, an indolent course, spontaneous remissions, low recurrence rate after therapy and infrequent dissemination.[4] Although not extensively reported, multifocal PCALCL tends to relapse more after systemic chemotherapy than the localized disease.[5] Our patient presented with localized lesions of PCALCL.

Clinical history

A 47-year-old Filipino female presented with a 1½-year history of two asymptomatic, well-defined, irregularly-shaped erythematous plaques at the medial aspect of right arm. These gradually enlarged and firm nodules developed within the plaques. Treatment with various topical medications afforded no improvement. Physical examination revealed two annular erythematous to violaceous indurated plaques with fixed nodules over the medial aspect of the right upper arm measuring 1.7 x 2.0 cm to 3.5 x 4.0 cm (Figure 1A). There were no lymphadenopathies or hepatosplenomegaly. Review of systems was unremarkable. She had no previous exposures to chemicals or toxic substances. Past medical history were negative for lesions of mycosis fungoides and lymphomatoid papulosis. Family history revealed a sister with breast cancer.

Laboratories showed normal complete blood count and

serum chemistries. Peripheral smear revealed no atypical lymphocytes. Chest xray, abdominal and thoracic computerized tomographies were negative for extracutaneous involvement. Skin punch biopsy showed dense infiltrates of non-epidermotropic, large, irregularly-shaped lymphocytes with hyperchromatic nuclei and mitoses extending from the superficial dermis to subcutaneous fat (Figures 2-4). Immunohistochemistry revealed that these atypical cells are ALK+, CD30+, CD3-, CD20- and EMA- (Figure 5). Clinical, histopathological and immunohistochemical findings were consistent with PCALCL.

Our patient was staged as T2aN0M0 based on the TNM classification system for primary cutaneous lymphomas other than mycosis fungoides (MF) / Sezary syndrome (SS) of the International Society for Cutaneous Lymphoma (ISCL) and Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC).[2] She was treated with five months of CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) chemotherapy achieving total resolution of skin lesions. Recurrence was noted after one year with a stage of rT1bN0M0. She underwent radiation therapy daily using Cobalt 60 with a dose of 40 Gy, using 1.25 MeV electrons for one month, achieving complete response (Figure 1B). Radiation therapy was well tolerated with still no evidence of disease at the most recent follow-up (18 months).

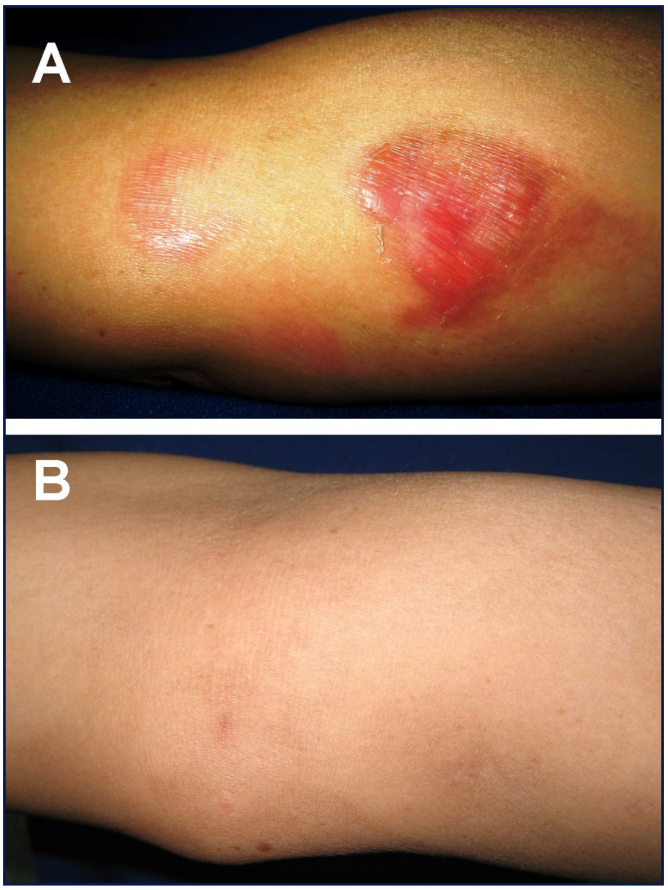

Figure 1

Close up view of the annular, erythematous to violaceous indurated plaques with fixed nodules over the medial aspect of the right upper arm (A). View afer therapy (B).

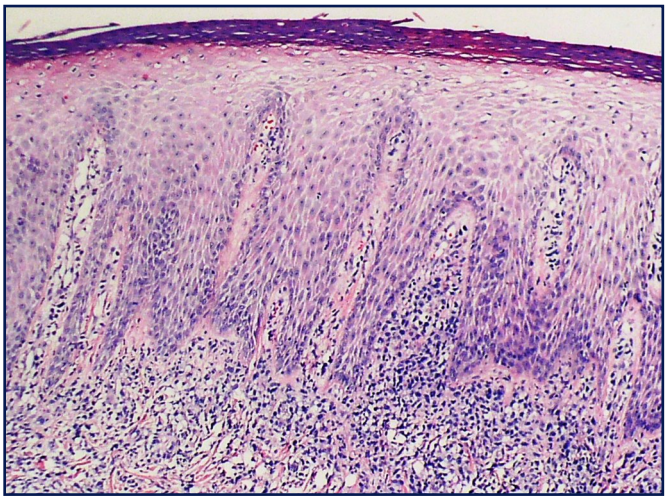

Figure 2

Photomicrograph of skin biopsy specimens taken from the indurated plaque showing dense diffuse infiltration of markedly atypical large lymphocytes throughout the dermis to subcutis, with epidermal hyperplasia and absence of epidermotropism. (hematoxylin-eosin stain, original magnification x 40)

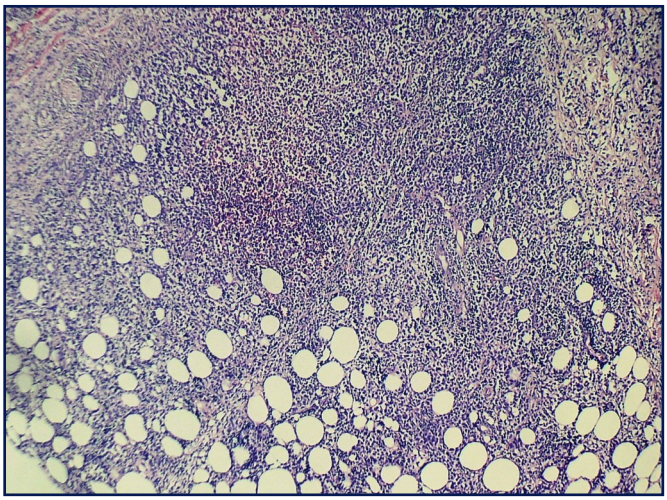

Figure 3

Photomicrograph of skin biopsy specimen showing atypical lymphocytes infiltrating up to the subcutaneous fat. (haematoxylin-eosin, original magnification x 40)

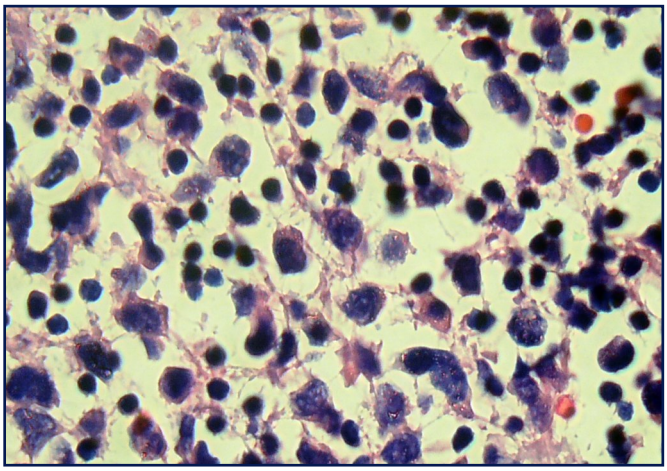

Figure 4

Most lymphocytes are large with irregular shapes and sizes showing hyperchromatic nuclei and frequent mitoses. (hematoxylin-eosin stain, original magnification x 40)

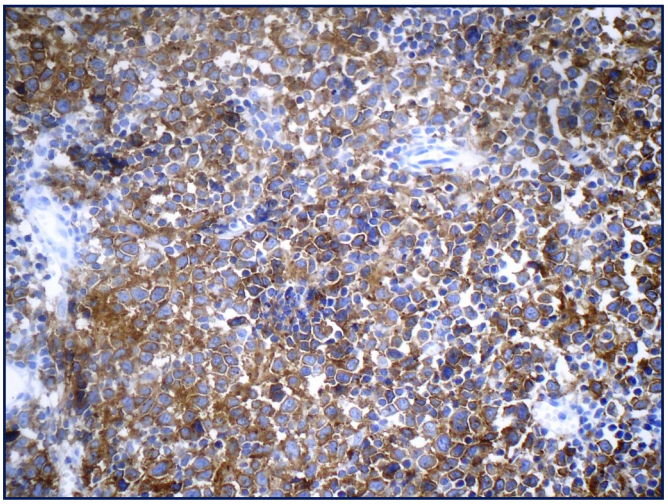

Figure 5

Note the appearance of many large anaplastic cells which are strongly positive for CD30. (Immunoperoxidase stain for CD30, original magnification x 40)

Discussion

Primary cutaneous T-cell lymphomas (CTCL) include clinically and biologically heterogenous group of non-Hodgkin lymphomas defined by clonal proliferation of skin-homing malignant T lymphocytes.[6] Primary cutaneous CD30+ lymphoproliferative disorders, accounts for 30% of the CTCL.[1] Under the group of primary cutaneous CD30+ lymphoproliferative disorders, the following diseases are included: primary cutaneous anaplastic large cell lymphoma (PCALCL), lymphomatoid papulosis (LyP) and borderline cases.

The criteria for the diagnosis of PCALCL include: (a) >75% infiltration of CD30+ large anaplastic cells in skin biopsy, (b) no clinical history of lymphomatoid papulosis, mycosis fungoides or other cutaneous lymphomas, (c) no extracutaneous localization after extensive investigations at presentation.[7] Our patient fulfilled all the criteria for PCALCL.

The mechanisms that are involved in the development of anaplastic large cell lymphoma are unknown.[8] In most patients, the initial step that involves activation and clonal expansion of CD30+ T cells is controlled effectively by the host immune response.[8] Further progression occurs only when the tumor cells acquire a growth advantage, either by additional chromosomal alterations or when the host immune response becomes deficient.[8] However, there may be spontaneous regression of the lesion if the host immune response is intact.[8]

PCALCL is characterized histologically with dense diffuse non-epidermotropic sheet-like infiltrates with cohesive sheets of large CD30+ atypical cells, known as "hallmark cells" comprising more than 75% of the cellular infiltrates. These are medium to large cells with kidney-shaped, hyperchromatic nuclei and prominent eosinophilic nucleoli and abundant cytoplasm. The infiltrates extend from the papillary dermis into the subcutaneous fat lobules.[4,7-13] Mitosis are frequent.[4,8-10]

PCALCL can be classified as: T-(CD3+), B-(CD20+) or null-(CD3-, CD20-) cell immunophenotype.[5,11,14,15] Since our patient is CD3- and CD20-, she is classified under null-cell type of PCALCL.

ALK is an independent predictor of survival which is associated with younger age, better response to chemotherapy and improved survival.[13,15-17] EMA is frequently expressed in systemic lymphoma and cutaneous involvement secondary to systemic ALCL.[10,11] CD30 is an activation antigen of lymphoid cells and also imparts a good prognosis.[7,8,15] Our patient has CD30+, ALK+, EMA- PCALCL connoting a good response to chemotherapy and good prognosis. The t(2;5)(p23;q35) translocation and its variants is rarely found in PCALCL.[1,6]

The appearance of large atypical cells on histopathology alone in patients with lymphoma does not always connote a poor prognosis. Immunohistochemical markers are essential to know the exact type of lymphoma because the prognosis will largely depend on this.

PCALCL usually presents as solitary asymptomatic reddish to violaceous nodule, plaque or tumor over the trunk and extremities occurring mostly in elderly males.[5,8,13-15] PCALCL is uncommon before age 20, with a peak at age 60.[4,14,15] It is about twice as common in men as in women, with a male to female ratio of 1.5 to 2.0:1.[8,14] Age, sex, ethnicity, extent of skin disease, primary lesion type, response to initial therapy and histologic morphology for PCALCL is not predictive of disease progression or worse survival.[14]

Our patient is classified as stage T2aN0M0 based on the TNM classification system for primary cutaneous lymphomas other than MF/SS of the ISCL/EORTC.[2] It has a favorable prognosis with 5- and 10-year survival rate of 91 to 100% and 68.6 to 78%, respectively.[1,8,11,14] Extracutaneous dissemination occurs in approximately 10% of patients with localized disease and mainly involves the regional lymph nodes, thus long-term follow-up is required in all patients with PCALCL.[8]

PCALCL is a chemosensitive and radiosensitive lymphoma. Treatment strategies include excision, local radiotherapy, CHOP chemotherapy (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) or combination of these modalities.[4,5,8,10,11,14,15] The overall complete response of PCALCL to CHOP therapy is 83%.[14] Our patient opted to be treated with five months of CHOP chemotherapy achieving complete resolution of lesions confirmed by histology. However, twelve months later recurrence was noted. Again, work-ups did not show any extracutaneous lesions. She then underwent radiotherapy and achieved complete remission.

Because the clinical presentation of PCALCL can be variable, a high index of suspicion is warranted in patients presenting with chronic plaques and nodules unresponsive to topical or oral medications.

References

1. Willemze R, Jaffe E, Burg G, *et al*. WHO-EORTC classification for cutaneous lymphomas. *Blood*. 2005; 105: 3768-3785.
2. Kim Y, Willemze R, Pimpinelli N, *et al*. TNM classification system for primary cutaneous lymphomas other than mycosis fungoides and Sezary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC). *Blood*. 2007; 110: 479-484.
3. Hung TY, Lin YC, Sun HL, Liu MC. Primary cutaneous anaplastic large cell lymphoma in a young child. *Eur J Pediatr*. 2008; 167: 111-113.
4. Tomaszewski M, Moad J, Lupton G. Primary cutaneous Ki-1 (CD30) positive anaplastic large cell lymphoma in childhood. *J Am Acad Dermatol*. 1999; 40:857-861.
5. Shehan J, Kalaaji A, Markovic S, Ahmed I. Management of multifocal primary cutaneous CD30+ anaplastic large cell lymphoma. *J Am Acad Dermatol*. 2004; 51:103-110.
6. Rosen S, Querfeld C. Primary cutaneous T-cell lymphomas. *Hematology*. 2006; 323- 330.
7. Gould J, Eppes R, Gilliam A, *et al*. Solitary primary cutaneous CD30+ large cell lymphoma of natural killer cell phenotype bearing the t(2;5)(p23;q35) translocation and presenting in a child. *Am Acad Dermatopathol*. 2000; 22(5): 422-428.
8. Willemze R, Meijer C. Primary cutaneous CD30-positive lymphoproliferative disorders. *Hematol Oncol Clin North America*. 2003; 17:1319-1332.
9. Farmer E, Hood A. Histopathology of Skin 2nd ed. Mc Graw Hill, 2000; 1375-1377.
10. Kumar S, Pittaluga S, Raffeld M, et al. Primary cutaneous CD30-positive anaplastic large cell lymphoma in childhood report of 4 cases and review of the literature. *Pediatr Dev Pathol*. 2005; 8: 52-60.
11. Mahalingam M, Bhawan J. Cutaneous anaplastic large cell lymphoma - a case report. *Indian J Dermatol Venereol Leprol*. 2004; 70: 168-171.
12. Kato N, Mizuno O, Ito K, *et al*. Neutrophil-rich anaplastic large cell lymphoma presenting in the skin. *Am J Dermatopathol*. 2003; 25(2): 142-147.
13. Stein H, Foss H, Durkop H, *et al*. CD30+ anaplastic large cell lymphoma: a review of its histopathologic, genetic and clinical features. *Blood*. 2000; 96(12): 3681-3695.
14. Liu H, Hoppe R, Kohler S, *et al*. CD30+ cutaneous lymphoproliferative disorders: The Stanford experience in lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma. *J Am Acad Dermatol*. 2003; 49: 1049-1058.
15. Hinshaw M, Trowers A, Kodish E, *et al*. Three children with CD30+ cutaneous anaplastic large cell lymphomas bearing the t(2;5)(p23;q35) translocation. *Pediatr Dermatol*. 2004; 21(3): 212-217.
16. Lee MY, Tsou MH, Tan TD, Lu MC. Clinicopathological analysis of T-cell lymphoma in Taiwan according to WHO classification: high incidence of enteropathy-type intestinal T-cell lymphoma. *Eur J Haematol*. 2005; 75: 221-226.
17. Sasaki K, Sugaya M, Fujita H, *et al*. A Case of primary cutaneous anaplastic large cell lymphoma with variant anaplastic lymphoma kinase translocation. *Br J Dermatol*. 2004; 150: 1202-1207.
18. Zackheim H, Vonderheid E, Ramsay D, *et al*. Relative frequency of various forms of primary cutaneous lymphomas. *J Am Acad Dermatol*. 2000; 43: 793-796.