JACOBS PUBLISHERS

OPEN ACCESS

Jacobs Journal of Radiation Oncology

Case Report

Indolent CD8+ Primary Cutaneous T-Cell Lymphoma of the Ear: A Case Report and Review of the Literature

LT Matthew J. Lail M.D.[*1,4],LCDR Steven J. Gauerke M.D.[2,4] ,CDR Edward F. Miles M.D[3,4]

[1]*Department of Radiology, Naval Medical Center Portsmouth, USA*

[2] *Department of Pathology, Naval Medical Center Portsmouth, USA*

[3] *Division of Radiation Oncology, Department of Radiology, Naval Medical Center Portsmouth, USA*

[4]*I am a military service member. This work was prepared as part of my official duties. Title 17 U.S.C. 105 provides that 'Copyright protection under this title is not available for any work of the United States Government.' Title 17 U.S.C. 101 defines a United States Government work as a work prepared by a military service member or employee of the United States Government as part of that person's official duties.*

Corresponding author: Dr. LT Matthew J. Lail, M.D., Department of Radiology,Naval Medical Center Portsmouth, 620 John Paul Jones Circle, Portsmouth, VA 23708, Tel: 704-763-0355; Fax: 757-953-6909; Email: mattjlail@gmail.com; Matthew.lail@med.navy.mil

Received: 08-13-2014

Accepted: 12-17-2014

Published: 03-26-2015

Abstract

Primary cutaneous peripheral T-cell lymphoma (PTL), unspecified, is a rare, heterogeneous group of lymphomas that do not conform to any of the more well defined subcategories of cutaneous T-cell lymphoma (CTCL) as defined by the 2005 World Health Organization (WHO)-European Organization for Research and Treatment of Cancer (EORTC) classification for cutaneous lymphomas. The prognosis for these neoplasms is generally poor, although one of three provisional subtypes is characterized by an indolent clinical nature (primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma [CSMPTCL]). There have been several case reports of what were suggested to be either a CD8+ variant of CSMPTCL or an entirely distinct subtype of CTCL, including cases with a curious predilection for the ears as well as the nose. We report a similar case of indolent CD8+ CTCL occurring on the left ear followed by a relapse on the right ear almost two years later.

Keywords: T-cell lymphoma; CD8; Ear; Indolent

Abbreviations:

CHOP	:Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone;
CTCL	:Cutaneous T-cell Lymphoma;
CSMPTCL	:Cutaneous Small/Medium Cell Pleomorphic T-Cell Lymphoma;
EBRT	:External Beam Radiation Therapy;
EORTC	:European Organisation for Research and Treatment of Cancer;
PTL	:Peripheral T-Cell Lymphoma;
WHO	: World Health Organization

Introduction

The term cutaneous T-cell lymphoma (CTCL) encompasses a diverse group of separate but related entities, united as clonal malignancies of T-cells with a predilection for skin tissue, but varying significantly in clinical presentation, immunohistochemical and genetic profiles, prognosis, and appropriate treatment modalities. CTCL represents approximately 75% of all primary cutaneous lymphomas and has an annual incidence of approximately 0.5 per 100,000 [1]. Primary cutaneous peripheral T-cell lymphoma (PTL), unspecified, is a rare, heterogeneous group of lymphomas that do not conform to any of the more well defined subcategories of CTCL as defined by the 2005 World Health Organization (WHO)-European Organisation for Research and Treatment of Cancer (EORTC) classification for cutaneous lymphomas. The prognosis for these neoplasms is generally poor, although one of three provisional subtypes is characterized by an indolent clinical nature: primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma (CSMPTCL) [2]. There have been several case reports [3-7] of what were suggested to be either a CD8+ variant of CSMPTCL or an entirely distinct subtype of CTCL, including cases with a curious predilection for the ears as well as the nose. We report a similar case of indolent CD8+ CTCL occurring on the left ear followed by a relapse on the right ear almost two years later.

Case Report

A 43-year-old Caucasian male presented in May 1998 with a one-month history of a 1.5cm soft mass on the helix of his left ear (case 1). A punch biopsy of the skin revealed a malignant T-cell lymphoma. Staging work-up revealed no evidence of other disease except a 1cm level II lymph node on the ipsilateral side that was not pathologically enlarged. At the time he was determined to be a clinical stage IAE and he was treated with combined chemotherapy and radiotherapy. He received three cycles of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) followed by external beam radiotherapy (EBRT) to the left upper neck and ear to a dose of 3600 cGy in 20 fractions. He completed all therapy in September 1998. He was doing well and on routine follow-up in February 2000 presented with a lesion on the right ear (case 2), which appeared similar to the original left-sided lesion. A punch biopsy again was consistent with peripheral T-cell lymphoma. He again underwent staging evaluation with no other evidence of disease. At this time it was decided to proceed with involved field radiotherapy (IFRT) alone, given limitations due to cardiotoxicity from doxorubicin. He received an additional 3600 cGy to the right ear, which was completed in April 2000. He is now 59 years old and being seen for follow-up annually, with no evidence of disease recurrence in over 14 years.

Materials and Methods

Original fixation, H&E staining, and microscopic examination were performed at the time of presentation and biopsy for each case, respectively. The cases were re-examined in 2012-2013 for the purposes of this report. Due to the age of the cases, blocks were not available, and prior negative control stained slides were decolorized and immunohistochemically stained.

Results

The morphology and immunohistochemical findings of case 1 and case 2 were virtually identical. Punch biopsies of the skin demonstrated extensive infiltration of the dermis by an atypical lymphoid infiltrate with sparing of the epidermis and adnexal structures. In case 1 no grenz zone was appreciated, and the sheet-like infiltrate extensively involved the deep margin with no discernible subcutaneous tissue. In case 2 a thin, clear-cut grenz zone was present and the subcutis was not involved. No necrosis, ulceration, or angiodestruction were identified. The lymphocytes were medium-sized and blast-like, with scant to moderate cytoplasm, irregular nuclear borders, open vesicular chromatin, and distinct nucleoli. Mitotic activity was brisk (1-2 figures per 40X high power field) (see Figure1). In both cases, immunohistochemical stains were strongly positive for CD3 and CD8 and negative for CD4, consistent with suppressor/cytotoxic T-cells (see Figure 2). Additionally, the tumor cells in case 1 were positive for CD45 and CD45R0 (see Figure 3) but negative for CD4 (see Figure 4), CD20 (see Figure 5), CD30, EMA, and S-100. The tumor cells in case 2 were notable for some positivity of CD20, but they lacked expression of CD30.

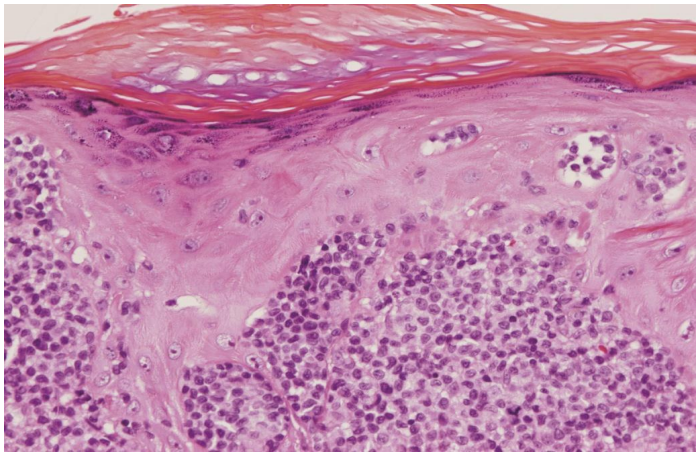

Figure 1. H&E, case 1, showing extensive lymphocytic infiltration of the dermis with sparing of adnexal structures (x40). A thin grenz zone is present in case 2.

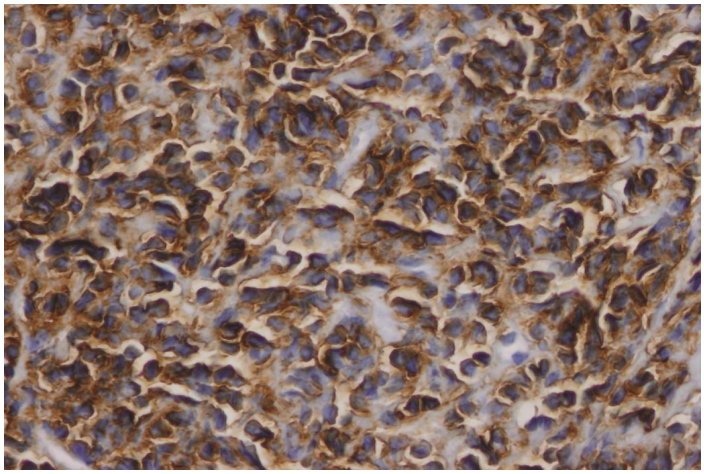

Figure 2. Immunohistochemistry demonstrating positivity for CD8, case 1 (x400).

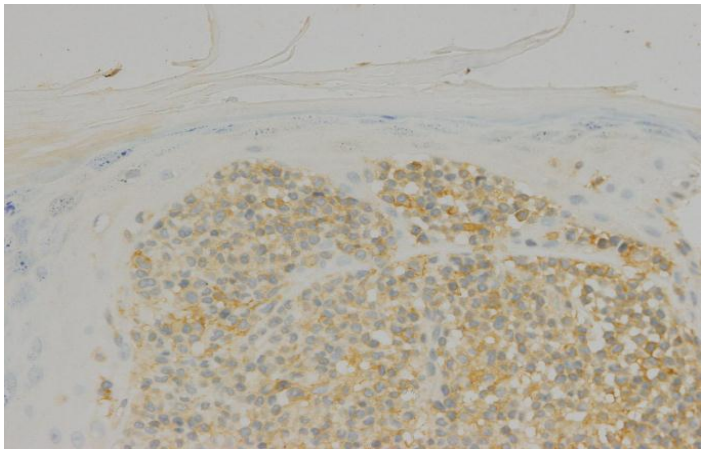

Figure 3. Immunohistochemistry demonstrating positivity for CD45R0, case 1 (x100).

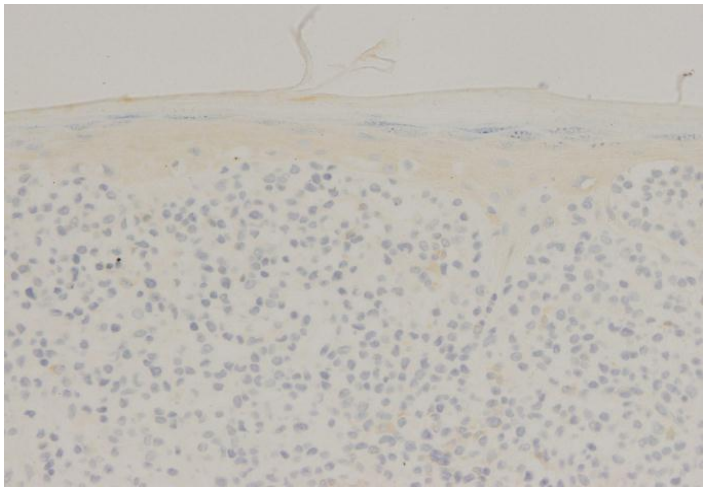

Figure 4. Immunohistochemistry demonstrating negativity for CD4, case 1 (x100).

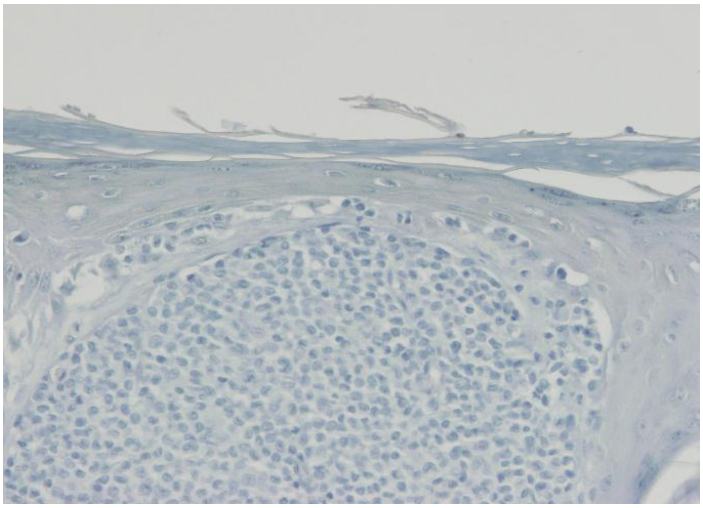

Figure 5. Immunohistochemistry demonstrating negativity for CD20, case 1 (x100).

Discussion

Given its indolent clinical nature, its lack of multiple patches, plaques, or other systemic findings, and its histologic, immunohistochemical, and molecular biological characteristics, we do not believe our case to belong in one of the already defined subtypes of CTCL which may express CD8, including: mycosis fungoides; primary cutaneous CD30+ lymphoproliferations such as primary cutaneous anaplastic large-cell lymphoma or lymphomatoid papulosis; pagetoid reticulosis; subcutaneous panniculitis-like T-cell lymphoma; hydroa vacciniforme-like CTCL; or the provisional entity, primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma [2]. Interestingly, the 2005 WHO-EORTC classification of cutaneous lymphomas did include a provisional entity, CSMPTCL, which appears similar to our case in certain aspects. However, these lymphomas by definition are characterized by a CD3+, CD4+, CD8-, CD30- phenotype [2]. The presence of CD8 positivity and absence of CD4 positivity in our case clearly prohibits its inclusion into the provisional category of CSMPTCL. Therefore, our case would be categorized as PTL, unspecified according to the current classification criteria.

A number of authors over the past several years, however, have provided a foundation of case reports upon which an argument can be made for addition of either a recognized CD8+ variant of CSMPTCL or possibly an entirely separate subtype of CTCL. In 2006, Khamaysi et al [6] described a case of "pleomorphic CD8+ small/medium size cutaneous T-cell lymphoma" occurring on the foot, suggesting its classification as a CD8+ variant of CSMPTCL. In 2007, Petrella et al. [3] described four cases of an indolent, CD8+ lymphoid proliferation involving the ears and suggested that this might represent a distinct entity that had not yet been defined by WHO-EORTC classification for cutaneous lymphomas. In 2010, Beltraminelli et al. [4] described

three cases similar to those of Petrella et al. [3] but emphasized that these might be more appropriately recognized as a phenotypic variant of CSMPTCL rather than a completely separate entity. Also in 2010, Ryan et al. [5] published yet another comparable case of a clinically indolent, CD8+ PTL, unspecified, occurring on the nose. The authors of this report remained impartial as to the best ultimate classification of these tumors and called for a collaborative review and the development of a consensus opinion on their most appropriate classification. Most recently, in 2012, Zeng et al. [7] reported two similar cases on the ear, contributing further to the growing body of reports of these tumors.

The clinical, morphologic, and immunohistochemical characteristics of our case are very similar to those of the cases described by the aforementioned authors. All cases involved presentation of a solitary, slowly progressive skin lesion typically found on the face, neck, or upper trunk, and with a frequent predilection for the ears. The tumor cell size was small-to-medium in all cases, and the lymphocytic infiltrate of the dermis was typically dense and diffuse. While length of follow-up has varied between these case reports, the overwhelming clinical trend has been one of indolence. Our case is somewhat unique in that the disease was bilateral with two years between the time of diagnoses, and it has one of the longest documented follow-up periods at over 16 years since initial diagnosis on the left ear and over 14 years since treatment of the right ear, with the patient doing well with no evidence of recurrence since that time.

Regardless of standpoint on the ultimate nomenclature and classification of these tumors, all of these authors have highlighted the critical importance of recognizing the clinical indolence of these lymphomas when determining the best management, whether with surgery, chemotherapy, radiotherapy, combined modalities, or simply observation. We hope that our case serves to emphasize yet again the indolent clinical nature of these tumors, as well as to provide further momentum toward and possible evidence for consideration of additions or changes in classification of these lymphomas.

References

1. Willemze R. Cutaneous T-cell lymphoma: epidemiology, etiology, and classification. Leuk Lymphoma. 2003, 44 (Suppl 3): S49-S54.

2. Rein Willemze, Elaine S Jaffe, Günter Burg, Lorenzo Cerroni, Emilio Berti et al. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005, 105(10): 3768-3785.

3. Petrella T, Maubec E, Cornillet-Lefebvre P, Willemze R, Pluot M et al. Indolent CD8-positive lymphoid proliferation of the ear: a distinct primary cutaneous T-cell lymphoma? Am J Surg Pathol. 2007, 31(12): 1887-1892.

4. Beltraminelli H, Müllegger R, Cerroni L. Indolent CD8+ lymphoid proliferation of the ear: a phenotypic variant of the small-medium pleomorphic cutaneous T-cell lymphoma? J Cutan Pathol. 2010, 37(1): 81-84.

5. Ryan AJ, Robson A, Hayes BD, Sheahan K, Collins P. Primary cutaneous peripheral T-cell lymphoma, unspecified with an indolent clinical course: a distinct peripheral T-cell lymphoma? Clin Exp Dermatol. 2010, 35(8): 892-896.

6. Khamaysi Z, Ben-Arieh Y, Epelbaum R, Bergman R. Pleomorphic CD8+ small/medium size cutaneous T-cell lymphoma. Am J Dermatopathol. 2006, 28(5): 434-437.

7. Zeng W, Nava VE, Cohen P, Ozdemirli M. Indolent CD8-positive T cell lymphoid proliferation of the ear: a report of two cases. J Cutan Pathol. 2012, 39(7): 696-700.