BRIEF ARTICLES

Recurrence of Primary Cutaneous Anaplastic Large Cell Lymphoma at a New Location After Wide Surgical Excision

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INTRODUCTION

Primary cutaneous anaplastic large cell lymphoma (PCALCL) and lymphomatoid papulosis (LyP) represent a disease spectrum of cutaneous CD30-positive lymphoproliferative disorders. Together, they are the second most common type of cutaneous T-cell lymphoma after mycosis fungoides. Histology of PCALCL reveals a dense dermal infiltrate of large T-cells with at least 75% of the tumor cells expressing the CD-30 antigen.[1] Prognosis is favorable with a 5-year survival rate ranging from 85-100%.[2,3] Clinical presentation is most often a solitary tumor; however multifocal disease with more than one lesion may occur. We report a case of a 54-year-old male with PCALCL manifesting as a tumor on the chest. Despite wide local excision with a depth down to the pectoralis major muscle, the disease recurred in the same area two months later.

CASE PRESENTATION

A healthy 54-year-old man presented with a several months history of an enlarging pink-red shiny nodule on his mid-chest with a few clustered satellite papules (Figure 1). He denied fever, fatigue, night sweats, weight loss, or a history of malignancy. Initial punch biopsies supported a diagnosis of reactive lymphoid hyperplasia. The tumor continued to enlarge and coalesce, reaching a size of 4.3 by 4.2 cm despite treatment with systemic, topical, and intralesional corticosteroids. Given the concern for a malignant process, the patient underwent wide local excision down to the pectoralis major muscle. The timing from the initial biopsy to excision was roughly 5 months. Histology of the excised specimen demonstrated a dense atypical lymphoid infiltrate in the dermis and subcutaneous tissue with a predominant population of large, CD3 and CD30-positive T-cells displaying nuclear atypia and abundant cytoplasm (Figure 3). P63 highlighted approximately 40% of the atypical T lymphocytes. TIA, granzyme, ALK and CD56 were negative. A second population of small, CD20-positive B-cells formed irregular lymphoid follicles, but were determined to be reactive due to a lack of clonality. Examined inked margins were negative for malignancy. The patient was sent for oncologic evaluation and a PET scan was negative for any metabolically active neoplasm. Patient denied a history of plaque or patch-like

lesions preceding this nodule. This history and a thorough skin examination helped exclude a pre-existing mycosis fungoides. Two months after excision, the patient presented with a new nodule on the right upper chest, several inches away from the initial site of occurrence (Figure 4). Shave biopsy confirmed recurrence of the tumor. The patient deferred radiation therapy and instead elected for serial skin examinations to monitor for growth. He was counseled on the probable need for radiation therapy in the future.

Figure 1. Initial Presentation of Two Enlarging and Pruritic Nodules on Patient's Chest.

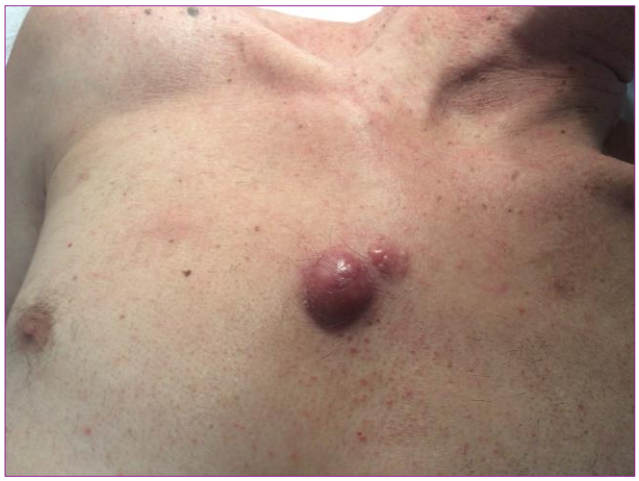


Figure 2. Pre-Excision Photo with Surgical Ink

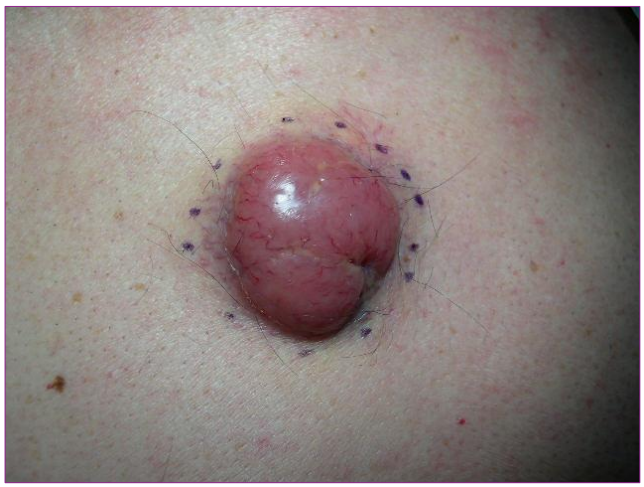


Figure 3. Stain Demonstrating An Abundance Of Atypical Lymphocytes (H&E, 40x)

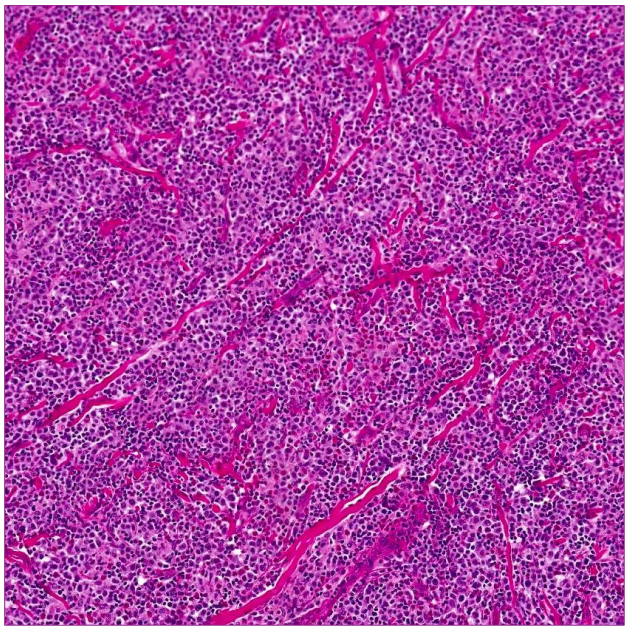
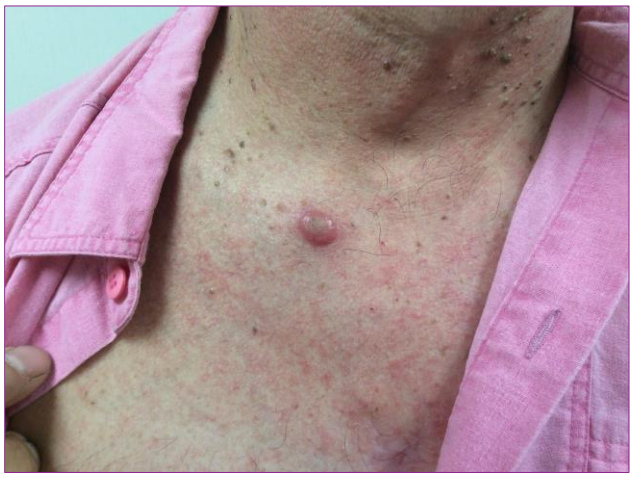


Figure 4. Recurrence of Tumor Two Months after Initial Excision.



DISCUSSION

The spectrum of CD30+ cutaneous lymphoproliferative disorders includes primary cutaneous anaplastic large cell lymphoma (PCALCL), lymphomatoid papulosis (LyP), and borderline CD30+ lesions.[4] Together, this group of disorders

accounts for 25-30% of all cutaneous T-cell lymphomas (CTCL). PCALCL is a neoplasm composed of large atypical lymphocytes characterized by the expression of cell-surface receptor CD-30 antigen, a marker for T-cell activation, in more than 75% of tumor cells.[2,5]

PCALC is an uncommon malignancy with an incidence of 0.1 to 0.2 per 100,000.[6] PCALCL is most commonly diagnosed in the sixth decade of life, with a slightly increased male to female ratio of 1.5 to 2:1. It is rare in children and adolescences.[4] Patients with PCALCL generally have an excellent prognosis with a 5-year survival rate ranging from 85-100%.[2,3] No clinical or histological factors have been found to be predictive of a worse outcome.[4] Partial or complete spontaneous regression is possible, but unlikely.

Patients may present clinically with solitary or multifocal papules and/or nodules usually affecting the upper half of the body, which may enlarge and ulcerate over time.[4] Roughly 10% of cases may present with multifocal cutaneous disease in multiple anatomic regions at the time of diagnosis.[7] Before a diagnosis of PALCL can be made, systemic anaplastic large cell lymphoma with secondary skin involvement must first be ruled out with imaging. Primary cutaneous disease has a better prognosis when compared to systemic disease with secondary cutaneous involvement.[7] CD30+ anaplastic large cell lymphomas can also develop secondarily from an aggressive transformation of mycosis fungoides, and is associated with rapidly fatal outcomes.[9]

The differential for PCALCL includes LyP, mycosis fungoides with large cell transformation, and reactive lymphoid hyperplasia. LyP typically presents with multiple widely distributed papulonodules that often spontaneously regress and recur. LyP type C in particular can be histologically nearly identical to PCALCL. Monoclonal rearrangement of T-cell receptor can be detected in LyP demonstrating the lack of T-cell clonality.[10] Therefore, differentiating between these two entities strongly relies on clinicopathologic correlation. Regardless, the delineation between PCALCL and LyP remains a diagnostic challenge.

Histological examination of PCALCL reveals a dermal infiltrate comprised of a dense infiltrate of large blast-like CD30-positive T-cells with pleomorphic nucleoli and abundant cytoplasm (Figure 3). CD30, also known as Ki-1, must be expressed by >75% of the tumor cells for diagnosis.[7] The anaplastic lymphoma kinase (ALK) gene, which demonstrates a nucleophosmin-ALK gene translocation, is typically, but not always, absent in primary cutaneous ALCL. In contrast, the ALK gene is often present in systemic ALCL.[7]

Surgical excision is the most common initial therapy used for solitary PALCL lesions, but studies have shown that relapses can occur in 43% of patients.[6] Time until recurrence ranges from 2-76 months, but most reported cases are unclear if relapse occurred at the original site or a new site.[6] No predictive marker for the risk of cutaneous relapse has yet been identified. Although our patient underwent extensive surgical excision (Figure 2), recurrence still occurred. Interestingly, the site of recurrence in our patient was not at the original tumor location, but approximately 8 cm away from the initial lesion. Some reports recommend an initial four to eight-week period of observation as PCALCL may regress spontaneously.[7] Radiotherapy, either alone or in combination with surgical excision is also an acceptable treatment for solitary lesions.[7]

Combination chemotherapy (with various regimens reported) has been the initial first-line treatment for multifocal primary cutaneous disease. Another possible approach to multifocal disease is anti-CD30 monoclonal antibody therapy. Brentuximab vedotin, an anti-CD30 antibody drug conjugate has been reported to effectively treat extensive disease.[6]

CONCLUSION

In summary, PCALCL is the second most common form of cutaneous T-Cell lymphoma. It can present as an enlarging solitary or multifocal nodule. Systemic anaplastic large cell lymphoma with secondary skin involvement must be ruled out with imaging. Treatment ranges from surgery, chemotherapy, and/or radiation depending on the number of lesions at presentation. However, despite treatment, relapse is common.

Abbreviations:
Lymphomatoid Papulosis (LyP)
Primary Cutaneous Anaplastic Large Cell Lymphoma (PCALCL)

Conflict of Interest Disclosures: None

Funding: None

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