

**PRIMARY CUTANEOUS CD30 +ANAPLASTIC
LARGE CELL LYMPHOMA; REPORT OF A SINGLE
LARGE SCALP NODULE**Isha Parulkar¹, Jason Micheals², Gladys H.Telang¹¹*Department of Dermatology, The Warren Alpert Medical School at Brown University, Providence, RI, USA*²*Private Practice, Aspire Dermatology. Riverside, RI, USA***Source of Support:**

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None

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Cite this article:Parulkar I, Micheals J, Telang GH. Primary Cutaneous CD30 +Anaplastic Large Cell Lymphoma; Report of a single large scalp nodule. *Our Dermatol Online.* 2014; 5(4): 434-436.**Case Report**

A 93-year -old Caucasian female presented with a 2-month history of a single frontal scalp nodule. The lesion was non-tender however had grown rapidly and was eroded with intermittent bleeding. There were no other skin lesions, lymphadenopathy, or hepatosplenomegaly. Past medical history was significant for breast cancer and review of systems was unremarkable. Physical exam revealed a 10cm x12cm exophytic, fungating, and malodorous tumor of the right frontal scalp (Fig. 1). A biopsy was performed and revealed a dense diffuse CD30+ atypical lymphoid infiltrate, ulceration, and inflammation. Within the dermis there were sheets of large epithelioid and anaplastic lymphocytes with large vesicular nuclei, prominent one to few magenta nucleoli and ample cytoplasm (Figs. 2 and 3). A few dermal mitoses and numerous neutrophils were present. The large anaplastic lymphocytes were diffusely CD30+ (Fig. 4) and Vimentin positive. CD3 and lymphocyte common antigen were negative. CD4 and CD8 stained approximately 60% and 30% of the T-cells, respectively. Less than 1% B-cells were present and stained positively with CD20 and PAX-5. CD15

highlighted approximately 20-30% positivity on neutrophils and CD68 stained approximately 10% histiocytes within the dermis. These findings supported the diagnosis of CD30+ anaplastic large cell lymphoma. The ALK-1 negativity favored primary cutaneous CD30+ anaplastic large cell lymphoma (PCALCL). Evaluation for underlying systemic disease was advised and the patient declined. Polymerase chain reaction (PCR) study to detect T-cell antigen Beta gene rearrangement showed one band consistent with the expansion of a single clonal T-cell proliferation. PCR was negative for immunoglobulin heavy chain gene rearrangement.

The clinical, histologic, immunohistologic, and PCR findings support the diagnosis of PCALCL. The patient was notified of her diagnosis and treatment options including excision, chemotherapy, and local radiation were discussed. She opted for no treatment and passed away two weeks later. Although an evaluation for systemic disease was not achieved, we present and discuss this case based on our clinical and pathologic diagnosis of PCALCL.



Figure 1. A large, exophytic, fungating tumor on the right frontal scalp.

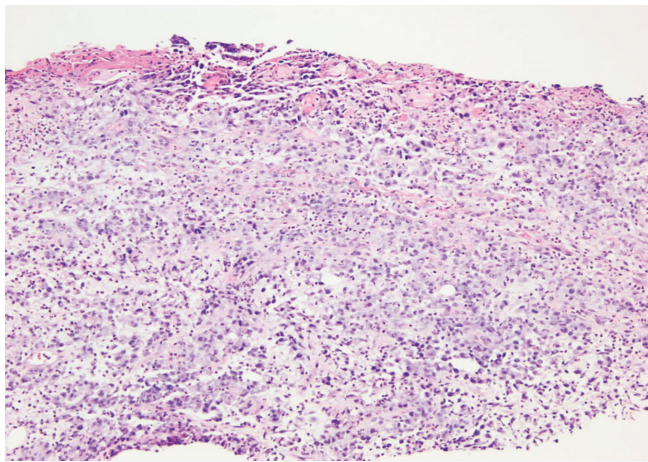


Figure 2. Sheets of large epithelioid and anaplastic lymphocytes with ample cytoplasm within the dermis. (hematoxylin eosin 10x)

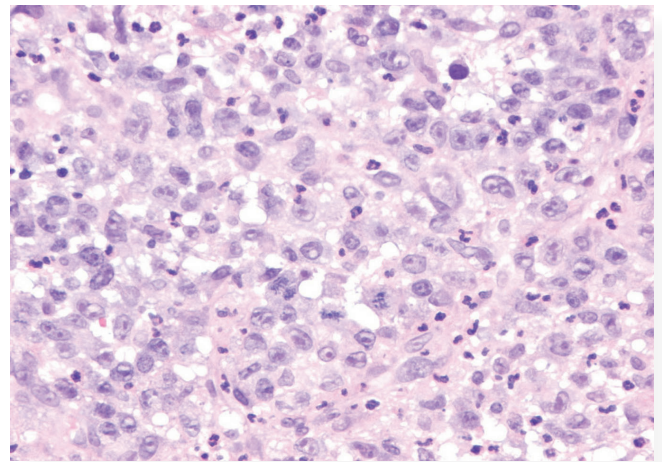


Figure 3. High power of the anaplastic and immunoblastic appearing lymphocytes, “hallmark cells”, with prominent mitoses. (hematoxylin eosin, 40x)

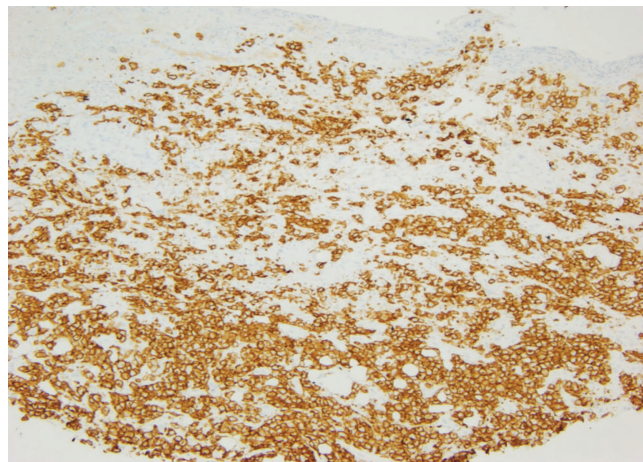


Figure 4. Numerous CD30 positive lymphocytes in dermis and subcutaneous fat. (immunoperoxidase stain, 10x)

Discussion

Primary cutaneous T-cell lymphomas (CTCL) are a clinically and histologically diverse group of non-Hodgkin lymphomas characterized by the aberrant proliferation of skin-homing T-lymphocytes. Together, they represent up to 75-80% of all cutaneous lymphomas [1]. Nearly a third of CTCL are accounted for by primary cutaneous CD30+ lymphoproliferative disorders, the most common subtypes of which are LyP (lymphomatoid papulosis) and PCALCL (primary cutaneous anaplastic large cell lymphoma) [2].

PCALCL are defined according to specific criteria: a) Predominance (>75%) of CD30+ large anaplastic cells on skin biopsy, b) absence of extracutaneous localization at presentation, c) no history or evidence of LyP, mycosis fungoides or cutaneous lymphoma [3,4].

The pathogenesis of PCALCL remains largely unknown [3]. A number of chromosomal imbalances (specifically gains on chromosomes 7q and 17q and losses on 6q and 13q) as well as amplification of several oncogenes have been found in patients with PCALCL [5,6]. The initial activation and clonal expansion of CD30+ T cells is thought to remain in check by an effective host immune response and can only progress when chromosomal alterations or a deficient host immune response

confers a growth advantage to cells [7]. Cases in which the immune response remains intact may result in spontaneous regression of the lesion [7].

PCALCL are twice as common in males as in females and tend to present in middle age with median age of 55 at diagnosis [3,7-8]. Clinically, they present as asymptomatic solitary or localized nodules, plaques, or tumors with central ulceration that favor the trunk and extremities. Extracutaneous involvement is rare (occurring in 10% of patients with localized disease), and regional lymphadenopathy, though infrequently seen, is not a predictor of prognosis [6,8]. Though biopsy is conclusive, imaging studies such as CT scan of the head, chest, and abdomen, are necessary to stage the disease and rule out systemic involvement [4].

The histopathology of PCALCL consists of cohesive aggregates or sheets of large CD30 antigen-expressing, atypical lymphocytes in the dermis and subcutaneous fat. Occasionally, epidermotropism may be present [6,10-11]. Rare morphological variants include angioinvasive, neutrophil-rich, histiocyte-rich, and sarcomatoid forms [12-14]. More than 75% of the cellular infiltrates are comprised of “hallmark cells,” so called because they are found in all types of anaplastic large cell lymphoma (ALCL) variants [11].

These lymphocytes are anaplastic, pleomorphic, or immunoblastic appearing, with abundant cytoplasm, frequent mitosis, irregular hyperchromatic and horseshoe-shaped nuclei and eosinophilic nucleoli [3,5,6,10]. Immunohistochemical screening reveals three immunophenotypes, the CD3+, CD4+ T-cell phenotype being the most frequent. Other subtypes include B-cell (CD20+) or null (CD3-, CD20-) [11]. A CD4+, CD3-, and CD20- phenotype was present in the case reported. Immunohistochemical markers are essential to characterize subtypes of ALCL and determine prognosis [3]. Expression of the anaplastic lymphoma kinase (ALK) gene, representing the t(2;5)(p23;q35) translocation is typically absent in PCALCL but often encountered in systemic ALCL [6,9]. Rare cases of ALK+ primary cutaneous ALCL have been reported and are associated with a more aggressive course, similar to systemic ALCL [15]. In contrast, CD30 antigen positivity imparts a good prognosis [3,7]. Epithelial membrane antigen (EMA) expression is seen more frequently in systemic lymphoma and cutaneous involvement secondary to systemic ALCL [3,16]. Treatment options include surgical excision, localized radiotherapy, topical nitrogen mustard therapy, single and multiagent chemotherapy (most commonly Cyclophosphamide, Doxorubicin, Vincristine, Prednisone or CHOP) [4,5,7]. Local radiotherapy is the treatment of choice for solitary lesions [7]. Patients with multifocal lesions may require more aggressive treatment modalities such as systemic chemotherapy. Multi-agent chemotherapy should be reserved for patients who develop extracutaneous or methotrexate-resistant disease [5,7,9]. Novel, less toxic, alternatives include Brentuximab, an anti-CD30 monoclonal antibody drug conjugate that is shown to be effective in patients unsuitable for multi-agent chemotherapy [17]. The rare cases of ALK+ PCALCL could be suitable for treatment with the ALK inhibitor Crizotinib [15]. Prognosis for PCALCL is typically excellent with 10-year disease related survival exceeding 90% [18]. Longitudinal care is recommended in patients given the 10% risk of developing systemic lymphoma [7].

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