SKIN

BRIEF ARTICLE

A Rare Case of Cutaneous Anaplastic Large Cell Lymphoma in an Adolescent Female

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ABSTRACT

Primary cutaneous anaplastic large cell lymphoma (C-ALCL) is a CD30 positive lymphoproliferative disorder, which is the second most common group of cutaneous T-cell lymphomas. It is common in adults 50-70 years of age with a male to female ratio 2:1. Here, we report a 14-year-old Caucasian female who presented with a painless, growing, friable, hemorrhagic nodule on her right medial buccal cheek of 2 weeks' duration. The lesion was traumatized during a basketball game and significant bleeding was noted. A shave biopsy was performed on the 1.7 cm x 1.3 cm lesion. Histopathology demonstrated epidermal necrosis, acanthosis, large, atypical lymphocytes with a number mitoses, prominent eosinophils, and smaller lymphocytes. Immunohistochemical staining revealed CD30 positivity of much of the tumor infiltrate but was not diffusely positive. Rare cells were granzyme positive. ALK-1, TdT, EBER, CD1a were negative. The diagnosis was confirmed by a second dermatopathologist. The patient was referred to oncology. Labs were within normal limits and PET/CT scan was negative for metastasis. The lesion started to spontaneously regress after the shave biopsy. Spontaneous regression of C-ALCL occurs in 20-42% of cases and usually has an indolent course, therefore, aggressive treatment is not appropriate. In most cases, solitary or localized lesions are treated with surgical excision or radiotherapy. Although, about half of cases reoccur, but are not life threatening. This unusual case of C-ALCL provides an additional example of a rare clinical presentation in an adolescent female and reiterates the important histopathological findings for diagnosis.

INTRODUCTION

Primary cutaneous anaplastic large cell lymphoma (PC-ALCL) is the second most common group of cutaneous T-Cell lymphoma's (CTCL), making up 25-30% of clinical cases.[1] PC-ALCL is a CD30 positive lymphoproliferative disorder that typically presents in 50 to 70-years- old with a male predominance of 2:1. The typical presentation of PC-ALCL is a solitary, or less commonly, a localized group, of nodules or papules that often ulcerate and persist for 3-4 weeks. Extracutaneous dissemination is a rare complication, occurring in 10% of cases, with the most common site being regional

lymph nodes.[2] This however does not confer a worse prognosis.

CASE REPORT

A 14-year-old Caucasian female presented with a growing, painless, friable, 1.7 cm hemorrhagic nodule on the right buccal cheek for two weeks (**Figure 1**). The patient stated the nodule was traumatized during a basketball game and experienced excessive bleeding. She was evaluated by urgent care and submental lymphadenopathy was noted on exam. The patient was prescribed oral antibiotics, but the lesion did not resolve.

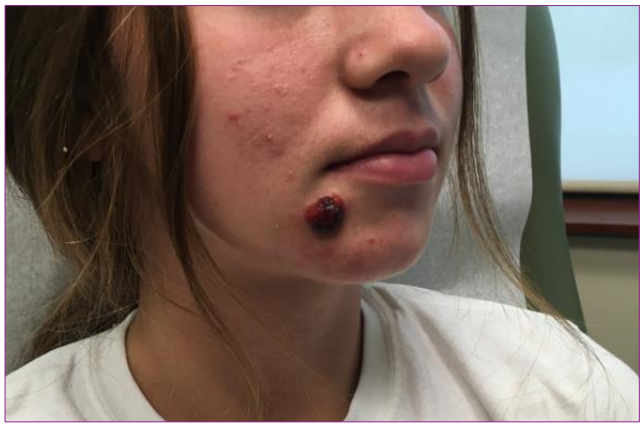

Figure 1. A 1.7 cm x 1.3 cm painless, growing, friable, hemorrhagic nodule on the right buccal cheek

A subsequent biopsy was performed. The histopathology demonstrated epidermal acanthosis with epidermotropism. In addition, overlying ulceration and necrosis was identified. There was an infiltrate extending to the dermal subcutaneous junction. The dermal infiltrate revealed large atypical lymphocytes with multiple irregular mitotic figures, pleomorphism, and prominent peripheral cytoplasm. Immunohistochemistry revealed prominent CD30 expression within the infiltrate. CD3 and CD4 were positive. The tumor was negative for TdT, EBER, CD1a, and ALK-1. CD56 and granzyme showed minimal expression within smaller lymphocytes.

The patient's histologic differential diagnosis included cutaneous anaplastic large cell lymphoma and lymphomatoid papulosis. Given the clinical presentation, the diagnosis of ALCL was favored. The patient was referred to pediatric oncology for further evaluation. The initial biopsied lesion had spontaneously regressed along with the submental lymphadenopathy. A PET/CT did not show any evidence of metastatic disease. Localized radiation and bone marrow biopsy was considered but no intervention was favored.

DISCUSSION

Primary cutaneous anaplastic large cell lymphoma is a CD-30 positive lymphoproliferative disorder. Following mycosis fungoides, it is the second most common subtype of cutaneous T-cell lymphomas. Many cases present in patients ages 50 to 70 years-old and are twice as likely to affect men than women. Clinically, solitary or localized nodules, tumors, or papules are seen and usually present on the upper half of the body. The lesions are often ulcerated and present for 3-4 weeks' duration. Multifocal lesions present in 20% of patients and extracutaneous dissemination occurs in 10% of cases, usually to regional lymph nodes, but does not confer a poor prognosis. The lesions can spontaneously regress, but up to half reoccur. This case was unique in that the presentation was in a 14 year- old female with a display of early, local lymph node involvement, despite displaying a single lesion.

Histologically, this tumor typically displays cohesive sheets of large cells with a pleomorphic, anaplastic or immunoblastic

cytomorphology.[3] The cells typically have round, oval or irregularly shaped nuclei, a prominent eosinophilic nucleolus, and abundant cytoplasm. It should also be noted that up to 25% of cases display Reed-Sternberg cells, further complicating the diagnosis. Immunophenotype is CD4 positive with or without CD3 and negative for CD2 and CD5. To make a diagnosis of PC-ALCL, CD30 must be expressed in most neoplastic cells. Also, while CD30 positivity is often presented in the setting of lymphocytic malignancies, it can also be observed in a wide variety of benign conditions including common viral infections, scabies, and atopic dermatitis.[8]

Differential diagnosis of PC-ALCL includes lymphomatoid papulosis (LyP), systemic ALCL, mycosis fungoides, and reactive lymphoid hyperplasia[6]. Immunophenotype serves as a helpful tool for the differentiation of these neoplasms. PC-ALCL can be differentiated from systemic ALCL as the neoplastic cells in ALCL do not express ALK-1[6]. Mycosis fungoides prototypically expresses CD3 and CD8, which can help distinguish this from PC-ALCL as PC-ALCL is CD8 negative. To differentiate PC-ALCL from reactive lymphoid hyperplasia, a lymph node biopsy can be beneficial, with the visualization of dohle bodies and tangible body macrophages within local lymph nodes. The most difficult differentiation to make lies between LyP and PC-ALC, as they have similar morphology and immunohistochemical profiles. Clinical clues can help the differentiation between these two neoplasms as LyP tends to be a recurrent, self-healing condition with small (<1cm) papulonodular skin eruptions. LyP also rarely displays pustular lesions or ulcers. In comparison, PC-ALCL tends to display larger skin lesions (>1cm) and ulceration is common. Spontaneous regression does occur in PC-ALCL, however, this is much less common and the majority of lesions do not regress. To further complicate this differential diagnosis, it is possible that there is overlap in these diagnoses as LyP can be concurrent to PC-ALCL or precede this neoplasm[3]. In the situation where a differentiation isn't possible, the tumors are denoted as "borderline".[7]

Once a diagnosis has been established, it is important to avoid overtreatment as PC-ALCL follows an indolent course and local lymph node metastasis does not confer a worse prognosis. If the lesions are localized, the primary approach is surgical excision and radiation [6]. In localized lesions where surgical excision is not possible, a low-dose oral methotrexate and local thermotherapy have been used with success.[8] Alternative treatment options in localized lesions of PC-ALCL include oral retinoids, with 13-cis-retinoic acid found to be the most efficacious.[8] If recurrence is observed multiple times or the nodules are multifocal and widespread, systemic therapy can be considered. In these cases, CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) has been used, however, it has not been shown to have improved outcome when compared to less aggressive treatments and recurrence is still seen.[6] Brentuximab vedotin, an anti-CD30 monoclonal antibody and anti-tubulin agent monomethyl auristatin, is FDA approved for relapsing systemic ALCL. It has been used in C-ALCL and MF expressing CD30, but not enough information is available to determine if it is beneficial.

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