BRIEF ARTICLE

Lymphocytoma Cutis – A Case Report

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ABSTRACT

Without tissue biopsy and holistic review of presentation, histology, and immunohistochemistry, lymphocytoma cutis (LC) can often be misdiagnosed as other benign conditions or malignant pathologies such as cutaneous B cell lymphoma (CBCL). A 36-year-old female presented with a two-year history of a progressive indurated, edematous plaque in the preauricular area. At presentation, the patient also had labs significant for thrombocytopenia and eosinophilia. Original treatment with topical steroids did not lead to clinical improvement of the lesions. Punch biopsy revealed reactive lymphoid hyperplasia with polyclonal lymphoid infiltrates of small lymphocytes, histiocytes, eosinophils, and plasma cells. Diagnosis of LC was made and our patient was treated with serial 5 mg intralesional triamcinolone injections. Clinical improvement was seen beginning at 2 months. Diagnosing LC can be particularly difficult as the clinical presentation is ubiquitous and can resemble several other conditions such as CBCL, cutaneous lupus erythematosus, sarcoid, or hypersensitivity reactions. Recognition of the typical histologic findings of top-heavy dermal mixed-cellular infiltrates along with polyclonal kappa and lambda hybridization on immunohistochemistry is often essential in arriving at the correct diagnosis. Following diagnosis of LC, long-term surveillance is recommended as malignant transformation is a possibility.

INTRODUCTION

Lymphocytoma cutis (LC) is a pseudolymphoma classically presenting in young females as solitary papules or plaques, most often on the face or along the hair line. Onset is insidious and asymptomatic. It is predominantly idiopathic; however, there are several known triggers of the condition.[1–3] For diagnosis, a histopathological and immunohistochemical analysis, are indispensable to exclude malignancies that manifest with analogous clinical features, notably Cutaneous B Cell Lymphoma. With proper treatment, the outcome is very favorable.

CASE REPORT

A 36-year-old female with history of eczema, acne vulgaris, iron-deficiency anemia, and thrombocytopenia presented with a 4 cm x 5 cm indurated, edematous plaque on the left preauricular area which was unresponsive to steroids **(Figure 1)**. Smoking, alcohol, family, and allergen history was unremarkable. The lesion initially appeared two years prior as a small keloidal-type scar with concomitant

eosinophilia (700 cells/uL). It was treated with 2.5% hydrocortisone cream. The patient was breastfeeding, so systemic medications were avoided. At follow-up one year later, a broad area of erythema and residual scarring had developed. Aclometasone was prescribed, but the lesion persisted and enlarged considerably into an erythematous, slightly indurated plaque. Punch biopsy of the left preauricular area revealed dense, diffuse, chronic inflammatory infiltrate of the dermis that appeared top-heavy, wedge-shaped, and composed predominantly of small lymphocytes **(Figure 2A and 2B)**. Histiocytes, numerous eosinophils, and plasma cells were also seen. Of note, eosinophilia resolved one month prior to biopsy (358 cells/uL).

Immunohistochemistry revealed a polyclonal lymphoid infiltrate of mixed CD3 (T cell) and CD20 L26 (B cell) population with one small germinal center of perifollicular CD20+ B cells highlighted by Bcl6 stain. T cells were highlighted by Bcl2. Plasma cells showed polytypic kappa and lambda *in situ* hybridization. Diagnosis of LC was made based on findings of reactive lymphoid hyperplasia.

Subsequent immunohistochemical analysis revealed the presence of a polyclonal lymphoid infiltrate, composed of a mixed population of CD3-positive T cells and CD20 L26-positive B cells. A discrete germinal center exhibiting perifollicular CD20+ B cells was prominently highlighted by the Bcl6 stain. Concurrently, the T lymphocytes were emphasized by the Bcl2 stain. The plasma cells exhibited polytypic immunoreactivity, evidenced by kappa and lambda in situ hybridization patterns. The constellation of these findings, indicative of reactive lymphoid hyperplasia, underpinned the definitive diagnosis of LC.

Treatment included 5 mg intralesional triamcinolone injection into the lower 1 cm of the lesion with subsequent follow-up for further evaluation and treatment. Clinical response was seen at 2 months with flattening and decreased erythema around the site of injection **(Figure 3)**. Since triamcinolone was tolerated with favorable results, the remainder of the lesion was also injected.

DISCUSSION

Lymphocytoma cutis represents a spectrum of benign lymphoproliferative reactions that can often resemble malignant cutaneous lymphomas in clinical presentation and/or histological assessment. The etiology of this condition can be stratified into four primary categories: infectious, drug-induced, reactions to foreign substances, and idiopathic.[1–3,9] Although idiopathic is most common, tattoo dyes and medications such as anticonvulsants, antipsychotics, CCBs, and biologic agents make up the largest percentage in cases with identifiable triggers.[9] The most common infectious agents are *Borrelia* sp., *Treponema pallidum*, HSV, VZV, poxvirus, scabies, and leishmaniasis.[2-3,9] This patient has a history of both iron deficiency anemia and thrombocytopenia. No cases have presented with thrombocytopenia and only one other case has reported iron deficiency anemia.[4] Skin examination often reveals erythematous pink-to-violaceous papules and nodules which can be shiny, usually without scale. In darker skin tones, it may appear as a red-brown color. It most often presents on sun-exposed areas. The rationale behind this proclivity for sun-exposed sites and any potential causative linkage with ultraviolet radiation remains an area of ongoing investigation.

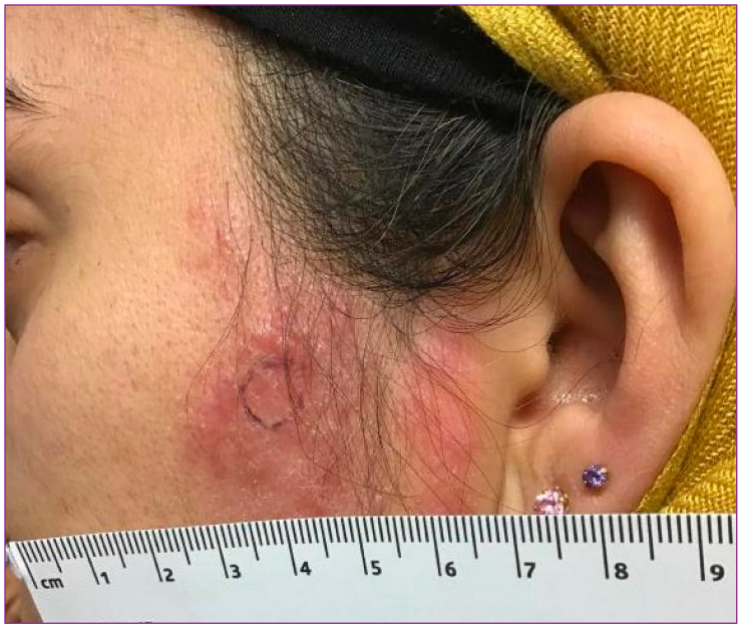

Figure 1. A 4 cm x 5 cm edematous plaque on left pre-auricular area prior to punch biopsy.

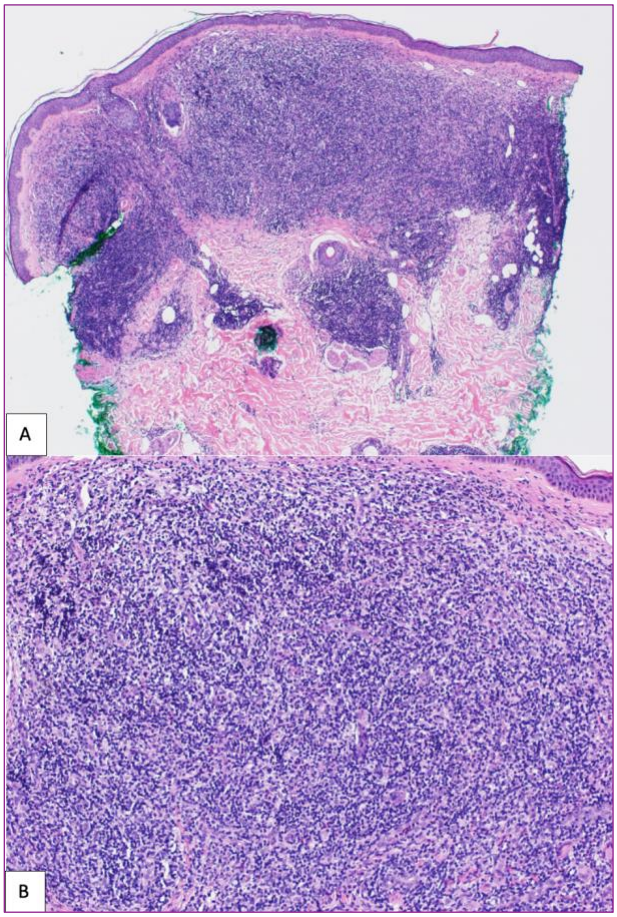

Figure 2A. The dermis shows dense diffuse chronic inflammatory infiltrate that is top heavy, wedge shaped. Prominent vasculature with increased number of thick-walled blood vessels with

plump endothelial cells. **B.** Infiltrate composed predominantly of small lymphocytes, with admixed histiocytes, numerous eosinophils, and plasma cells

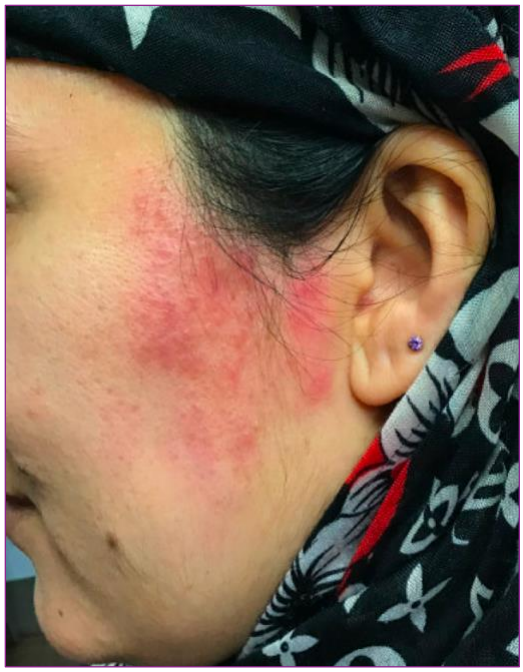

Figure 3. The lesion at 2 months follow-up shows flattening and decreased erythema in the inferior portion which received triamcinolone compared to the superior portion which was not injected at the initial treatment.

The diagnosis is not clinical as initial presentation is ubiquitous. A combination of physical exam, biopsy, histopathology, and immunohistochemistry is necessary to elucidate the diagnosis. The differential includes cutaneous lymphoma, cutaneous lupus erythematosus, sarcoidosis, and drug-induced hypersensitivity reaction. Priority should be in differentiating LC from cutaneous B cell lymphoma (CBCL). Clinical presentation is similar between the two; however, if there are multifocal lesions, CBCL should be favored. Biopsy is required to confirm the lesion is benign. On histology, LC can reveal a spectrum of nodular-to-diffuse, mixed-cellular infiltrates throughout the dermis with multiple foci of lymphocytes and an infiltrate of small lymphocytes, histiocytes, eosinophils, and plasma cells. The papillary dermis can have increased density of collagen.[5] The hallmark of LC is a lymphoid hyperplasia with mixed T and B cell predominance and a polyclonal lymphocytic population on immunohistochemistry.[2]

Histologically, LC appears top-heavy with polymorphous infiltrate, germinal centers, and eosinophils; CBCL appears more bottom-heavy and has monomorphic cellular infiltrate with atypia.[2] Immunohistochemistry also aids in differentiation. LC is polyclonal with both kappa and lambda in situ hybridization while CLBL will either have kappa or lambda hybridization.[2,3] Polyclonal versus monoclonal gene arrangement for LC and CBCL, respectively, can aid in the diagnosis if other characteristics are not apparent. However, there have been reported cases of monoclonal infiltrates in pseudolymphomas, so if morphology and immunohistochemistry favor LC, it should not be ruled out simply due to monoclonality.

Cutaneous lupus erythematosus and sarcoidosis can be dismissed via histopathologic assessment. Lupus lesions present as a perivascular infiltrate with epidermal involvement; sarcoid shows noncaseating granulomas with a mild fibrotic rim.[10,11] Both conditions frequently have secondary characteristics with involvement of other organs. LC is distinguished from drug-induced hypersensitivities by the rate of onset. Drug-induced occurs more acutely compared to the insidious onset of cutaneous pseudolymphomas. In addition, hypersensitivity syndrome may present with concomitant lymphadenopathy, organomegaly, or diffuse lymphadenopathy.

Cure is possible in most cases with proper treatment and follow-up. Any identifiable insulting drugs or irritants should be removed. Standard therapy includes topical or intralesional glucocorticoids, PUVA, surgical excision, topical calcineurin inhibitors, cryosurgery, cytotoxic agents, and/or hydroxychloroquine.[1–3,6-8] There is some controversy in the literature regarding first-line therapy, but many patients experience complete resolution with a short course of either topical or intralesional steroids. Patient follow-up is essential as several rounds of therapy are often needed to completely resolve the condition. A small number of cases have also reported evolution into cutaneous lymphoma, necessitating long-term surveillance.[3]

Lymphocytoma cutis is a benign pseudolymphoma differentiated from cutaneous B cell lymphoma and other differential diagnoses by clinical presentation, morphology, and immunohistochemistry. In-depth history is needed to identify possible causative agents. Idiopathic LC is often amenable to treatment with intralesional corticoids and can result in complete resolution of symptoms. The lesions should continue to be observed following treatment to monitor for malignant evolution.

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