Cutaneous Lymphoid Hyperplasia: A Case Report and Brief Review of the Literature

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GOAL
To understand cutaneous lymphoid hyperplasia (CLH) to better manage patients with the condition

OBJECTIVES
Upon completion of this activity, dermatologists and general practitioners should be able to:
1. Discuss the etiology of CLH.
2. Describe the histologic presentation of CLH.
3. Identify treatment options for CLH.

CME Test on page 462.

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Cutaneous lymphoid hyperplasia (CLH) is considered a benign lymphoid reactive process that results from various antigenic stimuli and may have potential for progression to overt lymphoma. CLH lesions may closely resemble lymphoma both clinically and histologically. We present a case of a 54-year-old woman who spontaneously developed lesions of unknown cause consistent with CLH. We also review the literature and discuss the etiology, clinical features, diagnosis, and management of CLH.


Case Report
An otherwise healthy 54-year-old woman presented with a 6-month history of multiple asymptomatic papules on her nose. The patient’s past medical history included hypertension and hyperlipidemia. Her medications included atenolol, hydrochlorothiazide, and gemfibrozil. She denied prior infection suggestive of *Borrelia* species or molluscum contagiosum. Results of a physical examination revealed 4 firm,
Cutaneous Lymphoid Hyperplasia

skin-colored to pink, dome-shaped papules on the right nasal ala (Figure 1) and dorsum. A shave biopsy of a lesion on the right nasal ala was performed. Results of a routine histologic evaluation revealed a diffuse basophilic infiltrate in the dermis (Figure 2). The infiltrate consisted of polyclonal B and T cells (Figure 3). The B cells were CD20⁺ and T cells were CD4⁺ and CD8⁺. In addition, there was a mixed expression of κ and λ chains within the infiltrate. The patient was diagnosed with cutaneous lymphoid hyperplasia (CLH).

For cosmetic reasons, numerous treatment modalities were attempted. The lesions initially were treated with a variety of topical steroids and immunomodulators, with minimal success. In addition, cryotherapy and intralesional steroids were used, with some short-lived response. However, the treated lesions never completely regressed and returned to their pretreatment size within 10 to 14 days after therapy. The lesions did respond well to shave removal, but the patient’s personal fear of needles prevented her from continuing this treatment option. She subsequently was lost to follow-up.

Comment
The term cutaneous lymphoid hyperplasia was coined by Caro and Helwig¹ in 1969. The disease also has been called lymphadenosis benigna cutis, Spiegler-Fendt pseudolymphoma, lymphocytoma cutis, and cutaneous lymphoplasia.² Although the pathogenesis of CLH remains unknown and most cases are idiopathic, certain drugs and long-term antigenic stimulation are implicated in many cases.³ Anticonvulsant medications (ie, phenytoin, phenobarbital, carbamazepine, sodium valproate) appear to be the most common pharmaceutical agents to cause CLH. Losartan, gemcitabine, bromocriptine, fluoxetine, amitriptyline, and injected silicone also have been associated with this disease.⁴⁻⁸ Rarely, infectious agents such as Borrelia species and molluscum contagiosum have been linked with CLH.⁹⁻¹¹ Additionally, CLH has occurred following exposure to various foreign antigens, including tattoos, trauma, body piercing jewelry, cobalt, leeches, and arthropod bites and stings.⁹⁻¹²⁻¹⁴ Appearance of multiple lesions has been reported following injection of allergen for hyposensitization.¹⁵,¹⁶ May et al¹⁶ described CLH localized to the site of influenza vaccination.

CLH is seen in both adults and pediatric patients and is 2 to 3 times more likely to occur in females.⁹ Morphologically, CLH appears as clusters of firm pink-colored to plum-colored papules, plaques, nodules, or tumors that occur on any skin surface but most commonly on the face. Although patients usually are asymptomatic, many seek treatment for cosmesis. CLH can be associated with regional lymphadenopathy, though most cases are not associated with other physical findings. The clinical differential diagnosis includes cutaneous lymphomas.¹⁰,¹⁷

On histologic examination, lesions of CLH may display multiple lymphoid follicles and dense superficial to deep infiltration of mostly mature lymphocytes.²,⁹ Lymphocytes often are admixed with histiocytes and occasional eosinophils and plasma cells.¹ Germinal centers with tingible body macrophages often are apparent.⁹,¹⁰,¹⁸ Because these features also may be seen in lymphomas, determination of polyclonality by immunophenotyping with either polymerase chain reaction or other techniques is helpful in the evaluation of CLH. Lesions of CLH may consist of an infiltrate that mostly consists of mixed CD4⁺ and CD8⁺ T lymphocytes in the periphery, with B lymphocytes predominating within germinal centers. Mixed expression of κ and
Cutaneous Lymphoid Hyperplasia

Lesions of CLH often regress spontaneously, though some cases become chronic and others recur locally. Rarely, some lesions progress to cutaneous lymphoma. However, it is uncertain if this represents true progression of a benign lesion along a continuum leading to lymphoma or a failure to diagnose a lesion that was malignant from the start.3,9,21

For CLH that results from known stimuli, the first step in treatment is removal of the causative agent. Antibiotic therapy has been effective in cases related to infective causes.10,18 Reported therapies for persistent or idiopathic cases include topical or intralosomal corticosteroids, cryosurgery, local radiation, excision, interferon alfa, and laser ablation.19,22,23 Good response to thalidomide has been documented in one small study.24

Conclusion

CLH is a benign lymphoid proliferation resulting from various antigenic stimuli and may have the potential for progression to overt lymphoma. Lesions may closely resemble lymphoma both clinically and histologically, highlighting the importance of immunophenotyping in establishing a diagnosis. Treatment of this benign disease entity needs to be individualized for each patient. Although there are numerous treatment options for CLH, none are consistently effective.

REFERENCES


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