Erythematous Papules on the Ears

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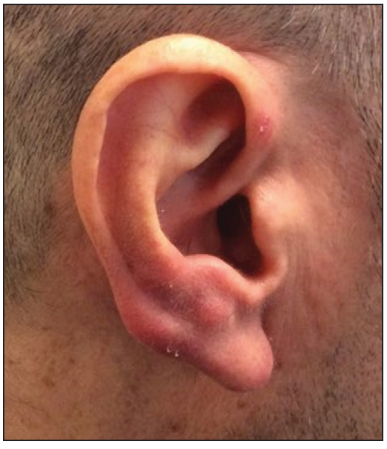
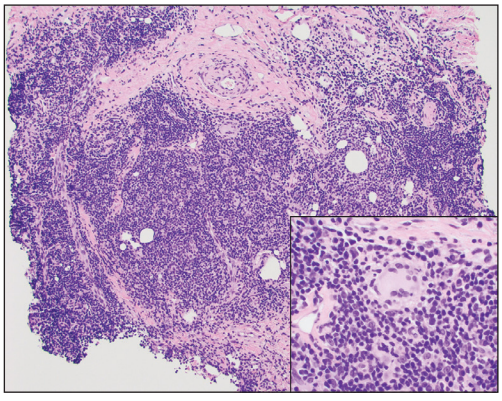


Erythematous and edematous nodules on the right ear.



H&E, original magnification ×200 (inset: H&E, original magnification ×100).

A 53-year-old man with a history of atopic dermatitis presented with pain and redness of the lobules of both ears of 9 months' duration. He had no known allergies and took no medications. He lived in suburban Virginia and had not recently traveled outside of the region. Physical examination revealed tender erythematous and edematous nodules on the lobules of both ears (top). There was no evidence of arthritis or neurologic deficits. A punch biopsy was performed (bottom).

THE BEST **DIAGNOSIS IS:**

a. arthropod bite reaction
b. borrelial lymphocytoma (lymphocytoma cutis)
c. diffuse large B-cell lymphoma
d. lymphomatoid papulosis
e. primary cutaneous follicle center lymphoma

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The authors report no conflict of interest.

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THE **DIAGNOSIS:** Borrelial Lymphocytoma (Lymphocytoma Cutis)

A punch biopsy revealed an atypical lobular lymphoid infiltrate within the dermis and subcutaneous tissue with a mixed composition of $CD3^+$ T cells and $CD20^+$ B cells (quiz image, bottom). Immunohistochemical studies revealed a normal CD4:CD8 ratio with preservation of CD5 and CD7. CD30 was largely negative. CD21 failed to detect follicular dendritic cell networks, and κ/λ light chain staining confirmed a preserved ratio of polytypic plasma cells. There was limited staining with B-cell lymphoma (Bcl-2 and Bcl-6). Polymerase chain reaction studies for both T- and B-cell receptors were negative (polyclonal).

Lyme disease is the most frequently reported vector-borne infectious disease in the United States, and borrelial lymphocytoma (BL) is a rare clinical sequela. Borrelial lymphocytoma is a variant of lymphocytoma cutis (also known as benign reactive lymphoid hyperplasia), which is an inflammatory lesion that can mimic malignant lymphoma clinically and histologically. Lymphocytoma cutis is considered the prototypical example of cutaneous B-cell pseudolymphoma.[1] Due to suspicion for lymphocytoma cutis based on the histologic findings and characteristic location of the lesions in our patient, Lyme serologies were ordered and were positive for IgM antibodies against p23, p39, and p41 antigens in high titers. Our patient was treated with doxycycline 100 mg twice daily for 3 weeks with complete resolution of the lesions at 3-month follow-up.

Clinically, BL appears as erythematous papules, plaques, or nodules commonly on the lobules of the ears (quiz image, top). Most cases of lymphocytoma cutis are idiopathic but may be triggered by identifiable associated etiologies including *Borrelia burgdorferi*, *Leishmania donovani*, molluscum contagiosum, herpes zoster virus, vaccinations, tattoos, insect bites, and drugs. The main differential diagnosis of lymphocytoma cutis is cutaneous B-cell lymphoma. Pseudolymphoma of the skin can mimic nearly all immunohistochemical staining patterns of true B-cell lymphomas.[2]

Primary cutaneous follicle center lymphoma frequently occurs on the head and neck. This true lymphoma of the skin can demonstrate prominent follicle centers with centrocytes and fragmented germinal centers (Figure 1) or show a diffuse pattern.[3] Most cases show conspicuous Bcl-6 staining, and IgH gene rearrangements can detect a clonal B-cell population in more than 50% of cases.[4]

Diffuse large B-cell lymphoma can occur as a primary cutaneous malignancy or as a manifestation of systemic disease.[4] When arising in the skin, lesions tend to affect the extremities, and the disease is classified as diffuse large B-cell lymphoma, leg type. Histologically, sheets of large atypical lymphocytes with numerous mitoses are seen (Figure 2). These cells stain positively with Bcl-2 and frequently demonstrate Bcl-6 and MUM-1, none of which were seen in our case.[4]

Lymphomatoid papulosis (LyP) tends to present with relapsing erythematous papules. Patients occasionally develop LyP in association with mycosis fungoides or other lymphomas. Both LyP and primary cutaneous anaplastic large cell lymphoma demonstrate conspicuous $CD30^+$ large cells that can be multinucleated or resemble the Reed-Sternberg cells seen in Hodgkin lymphoma (Figure 3).[4]

Arthropod bite reactions are common but may be confused with lymphomas and pseudolymphomas. The perivascular lymphocytic infiltrate seen in arthropod bite

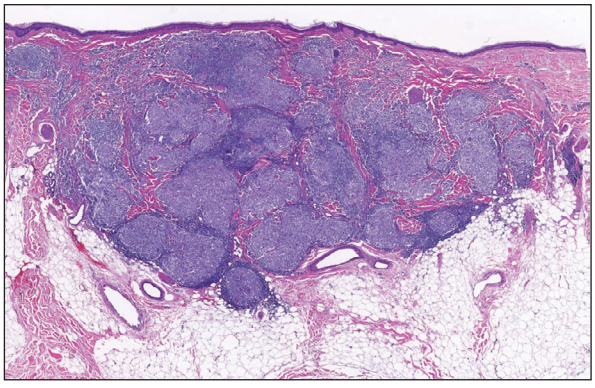

FIGURE 1. Primary cutaneous follicle center lymphoma. Dense nodular aggregates of atypical lymphocytes forming irregular germinal centers (H&E, original magnification ×20).

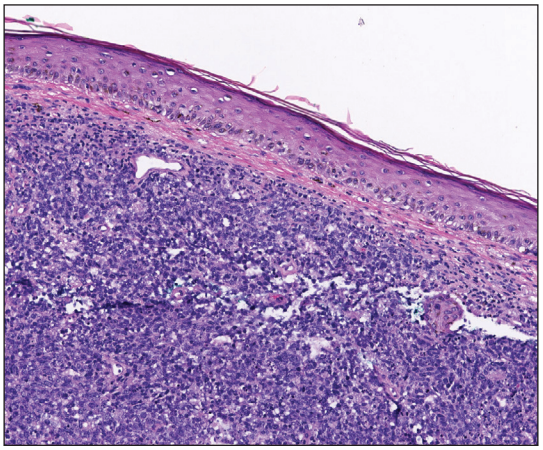

FIGURE 2. Diffuse large B-cell lymphoma. Sheets of large atypical lymphocytes separated from the epidermis (Grenz zone) by compacted collagen (H&E, original magnification ×40).

reactions may be dense and usually is associated with numerous eosinophils (Figure 4). Occasional plasma cells also can be seen, and if the infiltrate closely adheres to vascular structures, a diagnosis of erythema chronicum migrans also can be considered. Patients with chronic lymphocytic leukemia/lymphoma may demonstrate exaggerated or persistent arthropod bite reactions, and atypical lymphocytes can be detected admixed with the otherwise reactive infiltrate.[4]

Borrelia burgdorferi is primarily endemic to North America and Europe. It is a spirochete bacterium spread by the *Ixodes* tick that was first recognized as the etiologic agent in 1975 in Old Lyme, Connecticut, where it received its name.[5] Most reported cases of Lyme disease occur in the northeastern United States, which correlates with this case given our patient's place of residence.[6] Borrelial lymphocytoma cutis occurs in areas endemic for the *Ixodes* tick in Europe and North America.[7] When describing the genotyping of *Borrelia* seen in BL, the strain *B burgdorferi* previously was grouped with *Borrelia afzelii* and *Borrelia garinii*.[2] In the contemporary literature, however, *B burgdorferi* is referred to as *sensu stricto* when specifically talking about the strain *B burgdorferi*, and the term *sensu lato* is used when referencing the combination of strains (*B burgdorferi, B afzelii*, *B garinii*).

A 2016 study by Maraspin et al[8] comprising 144 patients diagnosed with BL showed that the lesions mainly were located on the breast (106 patients [73.6%]) and the earlobe (27 patients [18.8%]), with the remaining cases occurring elsewhere on the body (11 patients [7.6%]). The *Borrelia* strains isolated from the BL lesions included *B afzelii, Borrelia bissettii*, and *B garinii*, with *B afzelii* being the most commonly identified (84.6% [11/13]).[8]

Borrelial lymphocytoma usually is categorized as a form of early disseminated Lyme disease and is treated as such. The treatment of choice for early disseminated Lyme disease is doxycycline 100 mg twice daily for 14 to 21 days. Ceftriaxone and azithromycin are reasonable treatment options for patients who have tetracycline allergies or who are pregnant.[9]

In conclusion, the presentation of red papules or nodules on the ears should prompt clinical suspicion of Lyme disease, particularly in endemic areas. Differentiating pseudolymphomas from true lymphomas and other reactive conditions can be challenging.

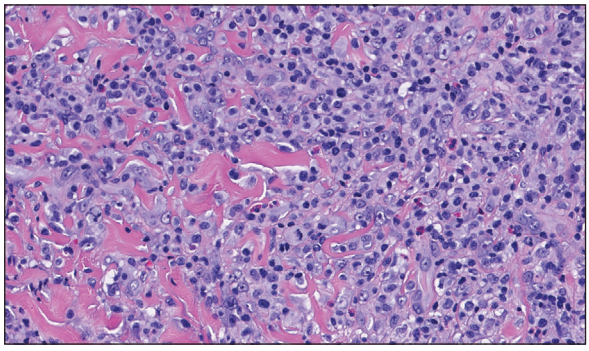

FIGURE 3. Lymphomatoid papulosis. Large pleomorphic lymphocytes with abundant pale cytoplasm, conspicuous mitoses, and scattered eosinophils in the dermis (H&E, original magnification ×400).

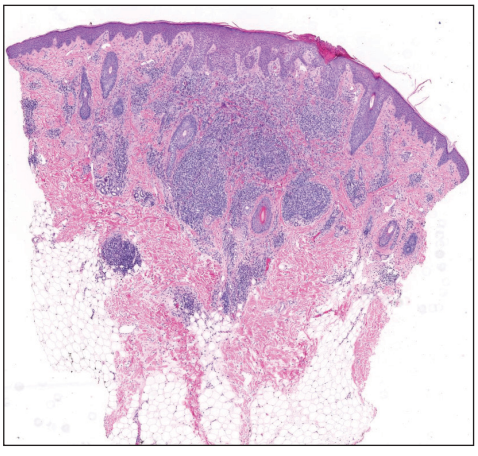

FIGURE 4. Arthropod bite reaction. Central area of scaly crust associated with mild spongiosis in the adjacent epidermis and mild papillary dermal edema. A wedge-shaped perivascular and interstitial mixed inflammatory infiltrate composed of lymphocytes, histocytes, and occasional eosinophils was noted in the dermis (H&E, original magnification ×20).

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