Asymptomatic Subcutaneous Nodule on the Cheek

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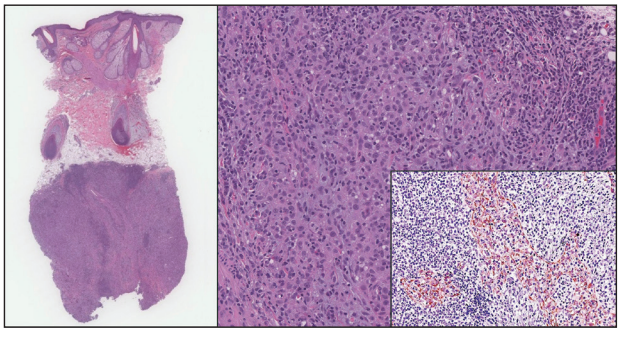

H&E, original magnification ×20 (left); H&E, original magnification ×200 (inset, cytokeratin, original magnification ×100)(right).

An 81-year-old man with history of melanoma and nonmelanoma skin cancer presented with a subcutaneous nodule on the left cheek of 3 months' duration. The lesion was reportedly asymptomatic and measured 2.6×2.9 cm. A punch biopsy of the lesion was obtained for histopathologic evaluation.

THE BEST **DIAGNOSIS IS:**

a. cutaneous lymphadenoma
b. lymphoepitheliomalike carcinoma of the skin
c. lymphomatoid papulosis
d. Rosai-Dorfman disease
e. squamous cell carcinoma

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THE **DIAGNOSIS:** Lymphoepitheliomalike Carcinoma of the Skin

The term *lymphoepitheliomalike carcinoma of the skin* (LELCS) initially was proposed by Swanson et al[1] in 1988 when they described 5 patients with cutaneous neoplasms histologically resembling nasopharyngeal carcinoma, also known as lymphoepithelioma. A PubMed search of articles indexed for MEDLINE using the term *lymphoepitheliomalike carcinoma of the skin* revealed over 60 cases of LELCS since 1988. However, unlike nasopharyngeal carcinoma, LELCS has not been associated with Epstein-Barr virus, with the exception of 1 known reported case.[2] The clinical appearance of LELCS is nonspecific but usually presents as a flesh-colored to erythematous nodule, as was seen in the current case. Lesions commonly are found on the head and neck in middle-aged to elderly patients with a slight male predominance.[2]

On histology, LELCS is characterized by aggregations of large, atypical epithelioid cells surrounded by a dense lymphoplasmocytic infiltrate (right quiz image). The neoplasm tends to reside within the deep dermis and/or subcutis[1] without appreciable epidermal involvement (left quiz image). The atypical epithelioid cells demonstrate positive immunoreactivity for cytokeratins (right quiz image inset), p40/p63, and epithelial membrane antigen,[3] and the surrounding lymphocytic infiltrate stains positively for leukocyte common antigen. The tumor histogenesis still is unknown, although an epidermal origin has been suggested given its staining pattern.[2] Other investigators have postulated on an adnexal origin, citing the tumor's dermal location along with case reports describing possible glandular, sebaceous, or follicular differentiation.[2,4]

Treatment for LELCS can include either standard surgical excision or Mohs micrographic surgery, with radiation reserved for lymph node involvement, tumor recurrence, or poor surgical candidates.[2,3,5] With appropriate therapy, prognosis may be considered favorable. Data from 49 LELCS patients presenting from 1988 and 2008 showed that 36 (73.5%) had no evidence of recurrence after treatment with standard surgical excision, 4 (8.2%) had local recurrence, and 6 (12.2%) developed lymph node metastasis, which led to death in 1 (2.0%) patient.[2]

Given the histologic similarity of LELCS to nasopharyngeal carcinoma, it is important to rule out the possibility of cutaneous metastasis, which can be done by testing for Epstein-Barr virus and performing either computed tomography imaging or comprehensive laryngoscopic examination of the head and neck region. In the current case, the patient was referred for laryngoscopy, at which time no suspicious lesions were identified. He subsequently underwent treatment with Mohs micrographic surgery, and the tumor was cleared after 2 surgical stages. At 5-month follow-up, the patient continued to do well with no signs of clinical recurrence.

Cutaneous lymphadenoma may be included in the differential diagnosis for LELCS on histopathology. This neoplasm is characterized by a well-circumscribed dermal proliferation of basaloid tumor islands within a fibrotic stroma (Figure 1). The basaloid cells may display peripheral palisading, and lymphocytes often are seen infiltrating the tumor lobules and the surrounding stroma (Figure 1 inset). Clinically, cutaneous lymphadenomas are slowly growing nodules that typically occur in young to

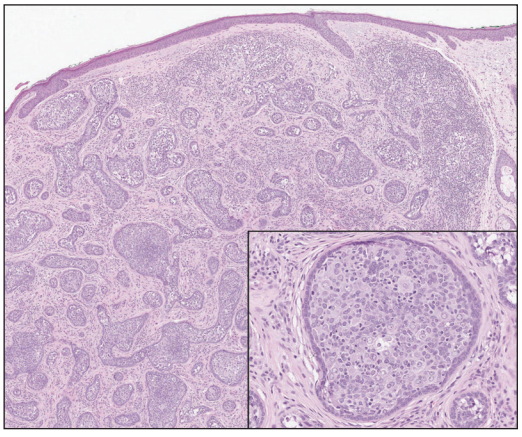

FIGURE 1. Lymphadenoma consisting of a well-circumscribed dermal proliferation of basaloid tumor islands within a fibrotic stroma and dense lymphocytic infiltrate (H&E, original magnification ×50 [inset, original magnification ×400]).

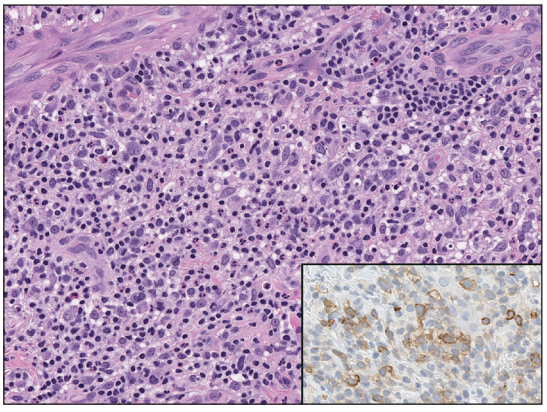

FIGURE 2. Type A lymphomatoid papulosis showing enlarged, pleomorphic lymphocytes with prominent nucleoli admixed with small lymphocytes (H&E, original magnification ×200). CD30 staining highlights large atypical lymphocytes (inset, original magnification ×200).

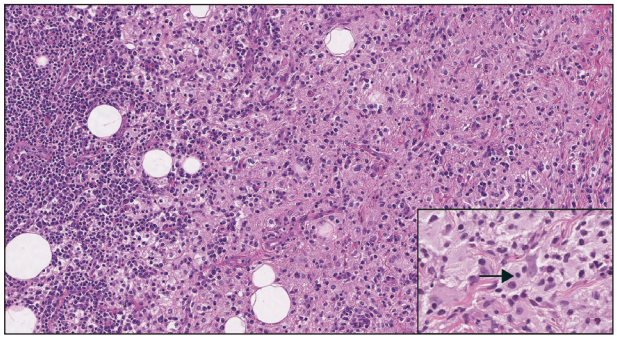

FIGURE 3. Rosai-Dorfman disease displaying atypical, pale-staining histiocytes admixed with a dense dermal infiltrate of inflammatory cells (H&E, original magnification ×200) and emperipolesis (arrow)(inset [H&E, original magnification ×400]).

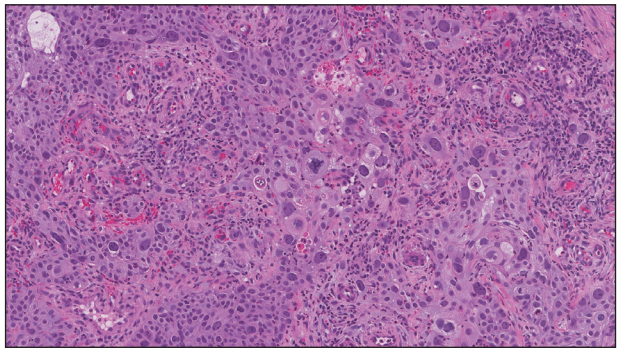

FIGURE 4. Squamous cell carcinoma with poorly differentiated, mitotically-active eosinophilic cells with surrounding suppurative inflammatory infiltrate (H&E, original magnification ×200).

middle-aged patients,[4,6] unlike LELCS, which is more commonly observed in middle-aged to elderly patients.[2]

The dense lymphocytic infiltrate seen in LELCS may obscure the neoplastic epithelioid cells and in doing so may mimic a lymphoproliferative disorder, such as lymphomatoid papulosis (LyP). Lymphomatoid papulosis is a chronic $CD30^+$ lymphoproliferative disorder consisting of recurrent crops of self-resolving papulonodules occurring on the trunk, arms, and legs. The average age of onset is in the third to fourth decades of life. Histology is dependent on the subtype; type A, the most common subtype, displays a wedge-shaped dermal infiltrate consisting of small lymphocytes (Figure 2) admixed with larger $CD30^+$ atypical lymphocytes with prominent nucleoli (Figure 2 inset).[7] Bizarre, binucleated forms resembling Reed-Sternberg cells also may be observed along with hallmark cells, which contain a horseshoe-shaped nucleus. The presence of admixed neutrophils and eosinophils also are common in type A LyP, a feature that is not characteristic of LELCS. Moreover, the atypical cells in LyP would not stain positively for epithelial markers as they would in LELCS.

Rosai-Dorfman disease is a rare condition that usually presents with painless cervical lymphadenopathy, typically in the first and second decades of life. Skin involvement can be seen in a small subset of extranodal cases, but cutaneous involvement alone is uncommon. On histopathology, cutaneous lesions are characterized by a dense dermal infiltrate of atypical histiocytes with vesicular nuclei and pale cytoplasm admixed with inflammatory cells, including lymphocytes, neutrophils, and plasma cells (Figure 3). Intracytoplasmic inflammatory cells or emperipolesis often is appreciated (Figure 3 inset).[8,9] The atypical histiocytes stain positively for S100 and negatively for CD1a.

Lymphoepitheliomalike carcinoma of the skin sometimes is considered to be a poorly differentiated, inflamed variant of squamous cell carcinoma (SCC).[10] A number of features may allow distinction of a primary cutaneous SCC from LELCS; for instance, SCC is more likely to have an epidermal connection and at least focal signs of squamous differentiation,[11] which can include the presence of poorly differentiated epithelial cells with mitoses (Figure 4), keratin pearls, dyskeratotic cells, or intercellular bridges.[12] Moreover, SCCs have a more variable surrounding inflammatory infiltrate compared to LELCS.

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