**Introduction**

Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare cutaneous neoplasm with low malignant potential. It is currently classified as a variant of squamous-cell carcinoma (SCC), although historically, its etiology has been debated. LELCS demonstrates nearly identical histologic features to undifferentiated nasopharyngeal carcinoma, also known as metastatic lymphoepithelioma of the nasopharynx, classically differentiated from LELCS by positive reactivity for an associated infection with Epstein-Barr virus (EBV). Therefore, an evaluation of the nasopharynx with an ear, nose, and throat (ENT) examination is advised to exclude undifferentiated nasopharyngeal carcinoma.

**Case Report**

An 83-year-old Caucasian female was referred to our dermatology clinic for surgical excision of a previously biopsied lesion on her left neck reported initially as a nodular basal-cell carcinoma with focal morpheaform features. The patient also complained of an asymptomatic, slowly enlarging lesion to her left parietal scalp believed to be present for at least three months. The patient’s past medical history was non-contributory, and she denied any constitutional symptoms at the time of clinical presentation.

Clinical examination revealed a solitary, 2.0 cm x 2.2 cm, tan to pink, indurated ulcerative plaque (Figure 1). There were no naso-oropharyngeal abnormalities or regional lymphadenopathy. A shave biopsy was performed to the left parietal scalp to exclude both basal-cell carcinoma and squamous-cell carcinoma.

The histopathological findings for both the left neck and left parietal scalp neoplasms showed a dermal proliferation of atypical epithelioid cells forming well-defined nests with a dense lymphocytic infiltrate (Figure 2). The atypical epithelioid cells were basophilic and featured enlarged nuclei with prominent nucleoli. A central ulceration was present under microscopic examination of the cutaneous biopsy on the patient’s left parietal scalp. The overlying epidermis appeared uninvolved in both samples. Each specimen stained positive for cytokeratin (CK) 5/6 and epithelial nuclear antigen (PNA) and negative for S-100 protein (Figure 3).
occurring on the trunk and upper extremity.7-9 The exposed areas, primarily the head and neck.2 occurs most often in elderly individuals on sun-

**Histology**

On histology, LELCS presents as a dermal proliferation of atypical polygonal epithelioid cells arranged in nests, cords, or sheets surrounded by a peripheral dense lymphocytic infiltrate.6 Cellular atypia includes vesicular hyperchromatic nuclei and prominent nucleoli with scant amphophilic-to-eosinophilic cytoplasm.2 The reactive lymphoid stroma is comprised of small B- and T-lymphocytes, staining positive for CD3 and CD20, with an occasional plasma cell present.4,5 LELCS generally extends into the reticular dermis with occasional involvement into the subcutis and even skeletal muscle.6,10 LELCS stains positively for pancytokeratin, CK5, CK6, p63 and EMA reactivity, likely indicating a neoplasm of epithelial origin.5,7 These markers also indicate that LELCS may derive from an epidermal, follicular, glandular, sudoriferous origin.2,6,7,11,14 In fact, the histogenesis of LELCS is controversial. Historically, LELCS was thought to derive from adnexal origin, supported by the fact that LELCS is located in the dermis and usually lacks a connection with the epidermis.2,15 Also, within LELCS, there is often sebaceous, eccrine and trichilemmal differentiation.2 In more recent literature, some consider LELCS to be a variant of squamous-cell carcinoma (SCC).6,14,16-20 For instance, Wang et al. presented a case of LELCS occurring below a scar from removal of multiple recurrent, well-differentiated and subsequent moderately differentiated SCC.19 However, SCC is typically located in the superficial dermis and maintains connectivity with the epidermis.2 Finally, others believe that LELCS is a morphologic pattern as opposed to a distinct clinicopathologic entity.17,20,21

**Differential**

The differential diagnosis is fairly extensive and includes cutaneous metastasis of undifferentiated nasopharyngeal carcinoma, a lymphoepithelioma-like carcinoma of another internal organ, basal-cell carcinoma, squamous-cell carcinoma, keratoacanthoma, Merkel-cell carcinoma, melanoma, malignant lymphoma, Hodgkin's lymphoma, cutaneous lymphadenoma, and follicular dendritic cell tumor.2,4 Histologic features and immunohistochemical staining distinguish LELCS from the possible differential diagnosis.

**Merkel-cell carcinoma** (MCC) can present clinically similar to LELCS but will stain positive for neuroendocrine markers such as synaptophysin, neuron-specific enolase, and CK20.7 In addition, peripheral lymphocytic infiltrate is usually absent in MCC.2,4 Clarke and Ioffreda report a case in which LELCS demonstrates spindle-shaped cells that resemble the spindle-cell variant of melanoma.23 However, unlike LELCS, melanoma is positive for S100 and other neuroendocrine markers such as HMB-45 and melan-A. LELCS should be distinguished from malignant lymphoma by the absence of atypical lymphocytes that will react positive in LELCS and negative in malignant lymphoma. LELCS has shown the presence of occasional binucleated cells resembling Reed-Sternberg cells; however, **Hodgkin lymphoma** is negative for cytokeratins and positive for CD30 and CD15.1,2,13,21 Basal-cell carcinoma will demonstrate neoplastic basophilic cells extending downward from the epidermis, whereas LELCS does not typically have an epidermal connection and lacks peripheral palisading. Inflamed, poorly differentiated squamous-cell carcinoma (SCC) strongly resembles LELCS.1,19 However, LELCS typically does not involve overlying epidermis, and poorly differentiated SCC usually has an area of well-differentiated carcinoma or overlying SCC in situ.1,2,5 Cutaneous lymphadenoma demonstrates a similar dense lymphocytic infiltrate as LELCS, but these lymphocytes appear benign and monomorphic.2,12 Follicular dendritic-cell tumor (FDCT) is similar to LELCS by way of syncytial-apparing plump cells surrounded by reactive lymphoid cells, but FDCT stains negative for cytokeratin markers.2 FDCT will demonstrate positive reactivity to Ki-M4, CD21, and CD35.2,4

Histologically, LELCS is remarkably similar to metastatic lymphoepithelioma of the nasopharynx, also known as undifferentiated nasopharyngeal carcinoma.1,15,21 Epstein-Barr virus (EBV) reactivity is the main distinguishing factor between LELCS and undifferentiated nasopharyngeal carcinoma.2,4,14 In general, LELCS is negative for EBV reactivity, whereas undifferentiated nasopharyngeal carcinoma will test positive for EBV.2,4,14 There has been only one reported case, that of a Japanese woman, of LELCS in a patient who tested EBV positive, but no related neoplasms were found elsewhere in the patient's body.22 In situ hybridization for EBER, the most reliable, specific, and highly sensitive method for detecting latent EBV, was used in this case report and yielded a negative result for EBV in our patient.22 In situ hybridization for EBER, the most reliable, specific, and highly sensitive method for detecting latent EBV, was used in this case report and yielded a negative result for EBV in our patient.22,23 Metastatic lymphoepithelioma of the nasopharynx is rare, but aggressive when it does occur.7-9 LELCS secondary to metastasis of undifferentiated nasopharyngeal carcinoma appears to be very rare, as there are fewer than 20 cases currently reported in the literature.2,4,11 Nonetheless, it is highly recommended to evaluate the patient for possible undifferentiated nasopharyngeal carcinoma by a complete otolaryngologic exam including indirect laryngoscopy of the nasopharynx.4,26 A review of symptoms is recommended when LELCS is confirmed to exclude metastasis from a variety of internal organ systems.2,4,5,22 Lymphoepithelioma-like carcinoma can be found in many organs besides the skin, including salivary glands, thyroid, thymus, lungs, stomach,
kidney, breasts, uterine cervix, prostate, vagina, and urinary bladder.\textsuperscript{4,5,7,14,17,23,27} Histologically, EBV reactivity has been associated only with lymphoepithelioma-like carcinoma of the stomach, salivary glands, lungs, and thymus.\textsuperscript{4,7,22,24}

**Treatment**

The prognosis for patients with LELCS is generally good despite its categorization as a poorly differentiated neoplasm.\textsuperscript{2,3,6,22,27} It is a low malignant tumor with rare reports of metastasis to lymph nodes at presentation and to internal organs such as, liver, lung, and bone.\textsuperscript{9,27} There are only two reported deaths from metastatic LELCS.\textsuperscript{6} There are multiple reports of local recurrence after incomplete excision.\textsuperscript{6} Therefore, most LELCS are treated by wide local excision or Mohs micrographic surgery, which is a preferred treatment modality for localized tumors. Radiation therapy and combined modality therapies are used in combination therapy for recurrent cases, nonsurgical candidates, and those with lymph-node metastasis.\textsuperscript{3,8} There are also a few reports of perineural invasion, in which Mohs micrographic surgery, radiation, and chemotherapy were used in combination therapy without evidence of recurrence on follow-up evaluation.\textsuperscript{4,7}

**Conclusion**

In conclusion, lymphoepithelioma-like carcinoma of the skin is a rare, slowly growing neoplasm with low malignant potential. LELCS is believed to be of epithelial origin based on immunohistochemical reactivity, although its exact histogenesis remains debatable. There are multiple dermatologic neoplasms that can clinically resemble LELCS. Therefore, it is important to conduct a histologic examination from a biopsied specimen to exclude other dermatologic entities. Undifferentiated nasopharyngeal carcinoma demonstrates identical histologic characteristics, and although it rarely occurs, it is a very aggressive neoplasm that requires a thorough otolaryngologic examination and CT scans of the head and neck if suspected. A thorough review of systems is recommended to exclude other possible organ systems that may have a lymphoepithelioma-like carcinoma metastasizing to the skin. Wide surgical excision or Mohs micrographic surgery are the recommended treatments for non-aggressive forms of LELCS to prevent local recurrence. To the best of our knowledge, this is the first case demonstrating two primary lymphoepithelioma-like carcinomas of the skin presenting in different anatomic locations on the same patient without evidence of a metastatic source.

**References**


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**LYMPHOEPITHELIOMA-LIKE CARCINOMA OF THE SKIN:**

**A CASE OF ONE PATIENT PRESENTING WITH TWO PRIMARY CUTANEOUS NEOPLASMS**