Lymphoepithelioma-Like Carcinoma of the Skin: 
A Report of Two Cases Treated With Complete 
Microscopic Margin Control and Review of Literature

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Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare cutaneous neoplasm with microscopic similarities to noncutaneous lymphoepitheliomatous malignancies, particularly undifferentiated carcinoma of the nasopharynx. It can be clinically and histologically confused with other benign and malignant tumors. If not adequately treated, recurrence and distant metastasis are probable. We present two cases of LELCS treated surgically with complete microscopic margin control (one by the Mohs method and the other with en face permanent sections) and review the literature.

Case Reports

Patient #1

A 97-year-old female presented with a 6-month history of an enlarging lesion of the cheek. Clinically a 2.0 × 2.2 cm red-violaceous, firm, dermal nodule was noted (Figure 1). There were no naso-oropharyngeal abnormalities or regional lymphadenopathy. The nodule was removed by Mohs micrographic surgery (MMS). The first stage of surgery revealed an infiltrating dermal tumor formed by large irregularly shaped nests of epithelial cells, with discrete nests observed in the subcutis (Figure 2, A and B). Tumor cells had basaloid morphology and a superficial resemblance to basal cell carcinoma. Tumor cells lacked peripheral palisading of nuclei, retraction artifact or mucinous stroma differentiating it from a basal cell carcinoma.

Figure 1. Red, shiny nodule on the left cheek consistent with lymphoepithelioma-like carcinoma.

Figure 2. (A) Infiltrating dermal tumor with large irregularly shaped nests of epithelial cells (toluidine blue, 10 × original magnification). (B) A nest of neoplastic cells with pleomorphic and vesicular nuclei and numerous large, abnormal mitoses. A dense infiltrate of lymphocytes and plasma cells are present at the periphery of the neoplastic cells (toluidine blue, 40 × original magnification).

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carcinoma. Larger, more pleomorphic cells were present focally. Several mitoses were easily identified. A dense infiltrate of lymphocytes and plasma cells was present at the periphery of the epithelial nests. Occasional central necrosis and keratinization within the tumor nests was apparent. Immunohistochemical staining of epithelial cells showed positivity for cytokeratin as well as epithelial membrane antigen (Figure 3). Cytokeratin-20 and anti-chromogranin labeling were negative, ruling out neuroendocrine carcinoma. A diagnosis of lymphoepithelioma-like carcinoma was rendered. Tumor-free margins were achieved after two stages and the defect was closed primarily. The patient died 6 months later of unrelated causes, with no evidence of recurrent tumor.

**Patient #2**

An 88-year-old female presented with a 2-year history of a progressively enlarging nodule on her left arm (Figure 4). On examination a non-tender, 2.3 × 1.9 cm erythematous-to-violaceous nodule was noted. There was no evidence of lymphadenopathy and the patient denied any constitutional symptoms. The lesion was excised with 5 mm margins, and sent for en face permanent sections oriented by the surgeon. Microscopically, multiple cords of anaplastic cells with a high nuclear:cytoplasmic ratio, vesicular nuclei, and variable large nucleoli were seen, consistent with lymphoepithelioma-like carcinoma with negative histological margins. A dense lymphoid infiltrate was noted in the background. The defect was repaired primarily.

**Discussion**

LELCS is an uncommon cutaneous neoplasm typically presenting as a flesh-colored or red, firm nodule or plaque. This tumor favors the head and neck region, but has been reported to occur on the trunk as well. LELCS affects middle aged to elderly patients and occurs in equal incidence in men and women.

LELCS histologically resembles the lymphoepitheliomatous malignancies that have been described to occur in the nasopharynx, palatine tonsils, salivary glands, lung, thymus, gastrointestinal tract, kidney, ureter, urinary bladder, breast, and uterine cervix. Microscopic examination reveals a multifocal distribution of tumor involving the mid to reticular dermis and occasionally the subcutis and skeletal muscle. Tumor cells are arranged in nodules and in isolated or anastomosing islands of trabeculae, narrow cords, and round to oval nests. The epithelial component of the tumor is composed of atypical polygonal cells with vesicular nuclei and prominent nucleoli. There is no connection between tumor and overlying epidermis or
dermal appendages. A dense infiltrate of lymphocytes and plasma cells surrounds the tumor islands in the dermis.\(^3\)

The differential diagnosis includes Merkel cell tumor, squamous cell carcinoma, pseudolymphoma, malignant lymphoma, melanoma, and metastatic lymphoepithelioma. Immunohistochemical assays are used to distinguish LELCS from other diseases.\(^1,20,22–24\) The atypical polygonal cells of LELCS show immunohistochemical staining for high-molecular weight cytokeratins and epithelial membrane antigen, indicating the epithelial nature of the neoplastic cells. Surrounding inflammatory cells stain with various T- and B-cell markers. Lymphoepithelioma-like carcinomas (LELC) are diverse in their expression of Epstein–Barr virus (EBV)-related nucleic acid. Unlike some noncutaneous LELC,\(^25\) recent studies show that LELCS does not contain the genomic DNA of EBV.\(^1,20\) LELCS is likely a neoplasm of adnexal differentiation based on the presence of sebaceous, eccrine and trichilemmal differentiation within the tumor. However, various authors have suggested that LELC may represent a morphological pattern rather than a distinct clinicopathologic entity.\(^26,27\)

Management of LELCS should include a thorough otolaryngological examination, including indirect laryngoscopy to exclude metastatic lymphoepithelioma of the nasopharynx.\(^3\) Effective treatment includes complete surgical removal with wide local excision or complete margin control utilizing MMS when available.\(^2,28–30\) There are four reports to date of LELCS treated with MMS, and we add another case to the literature. The clinical data of LELCS patients treated with the Mohs technique are presented in Table 1. When MMS is unavailable, the surgeon may consider the use of en face permanent sections to ensure complete margin examination as seen with Patient 2.

Despite its poorly differentiated histology, LELCS prognosis is relatively good. However, recurrences from incomplete excision, metastasis to regional lymph nodes, and one case of fatal distant metastasis have been reported.\(^1,22\) The tumor appears to be radiosensitive as seen in nasopharyngeal lymphoepithelioma, but because of the risk of metastasis in inadequately treated tumors, X-ray therapy should be reserved for those patients who are not surgical candidates or adjunctive therapy in aggressive or unresectable tumors.\(^1,22,31,32\)

### References


### Table 1. Clinical Features of Patients Treated with Mohs Micrographic Surgery

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Presentation</th>
<th>Location</th>
<th>Management</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>97</td>
<td>F</td>
<td>2 cm nodule</td>
<td>Left cheek</td>
<td>MMS</td>
<td>NED, after 6 mo</td>
</tr>
<tr>
<td>Patient 2</td>
<td>88</td>
<td>F</td>
<td>2 cm nodule</td>
<td>Left arm</td>
<td>Wide excision with en face permanent section margin control</td>
<td>NED after 10 mo</td>
</tr>
<tr>
<td>2</td>
<td>74</td>
<td>F</td>
<td>Nodule</td>
<td>Left cheek</td>
<td>MMS</td>
<td>NED, unknown duration</td>
</tr>
<tr>
<td>3</td>
<td>81</td>
<td>M</td>
<td>2 cm nodule</td>
<td>Left side mandible</td>
<td>MMS</td>
<td>NED, unknown duration</td>
</tr>
<tr>
<td>28</td>
<td>91</td>
<td>F</td>
<td>0.4 cm papule</td>
<td>Left dorsal nose</td>
<td>Electrodesication and curettage; MMS at time of recurrence</td>
<td>Recurrence after 1 mo NED 20 after MMS</td>
</tr>
<tr>
<td>29</td>
<td>68</td>
<td>M</td>
<td>1.8 cm plaque</td>
<td>Left nasal ala</td>
<td>MMS</td>
<td>NED 12 mo</td>
</tr>
</tbody>
</table>

F, female; M, male; MMS, Mohs micrographic surgery; mo, month; NED, no evidence of disease.


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