

# Lymphoepithelioma-like Carcinoma of the Skin: A Case with Perineural Invasion

Cecilie B. Lassen, MD  
Jørgen Lock-Andersen, MD,  
DSci

**Summary:** Lymphoepithelioma-like carcinoma of the skin is a rare, low malignant cutaneous neoplasm. We report a case of an elderly woman with lymphoepithelioma-like carcinoma of the skin in the forehead. The tumor was mistaken first as actinic keratosis and later as metastatic squamous cell carcinoma. A histological reassessment showed lymphoepithelioma-like carcinoma of the skin with perineural invasion, which is rare and considered more aggressive. The patient therefore received adjuvant radiotherapy after the recommended wide excision. Lymphoepithelioma-like carcinoma of the skin is a variant of squamous cell carcinoma, and histologically, it resembles the more aggressive lymphoepithelioma of the nasopharynx. The later is Epstein-Barr positive, whereas lymphoepithelioma-like carcinoma normally is not. Lymphoepithelioma-like carcinoma is an important diagnosis to know and the disease is discussed. (*Plast Reconstr Surg Glob Open* 2014;2:e252; doi: 10.1097/GOX.0000000000000215; Published online 12 November 2014.)

Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare cutaneous neoplasm of unknown etiology.<sup>1</sup> It is related to lymphoepithelioma-like carcinoma, which can occur in many organs.<sup>2</sup> LELCS was first described in 1988 by Swanson et al<sup>3</sup> and since approximately 70 cases in the English literature have been reported.<sup>1,4-6</sup> LELCS is a variant of squamous cell carcinoma, and histopathologically, it is related to lymphoepithelioma of the nasopharynx (undifferentiated nasopharyngeal carcinoma).<sup>4,7</sup> It is a malignant tumor with low metastatic risk. Normally, it is treated with surgery, but more aggressive LELCS, including LELCS with perineural invasion, has also been treated with radiation and chemotherapy.<sup>5</sup>

In this article, we present a case of LELCS with perineural invasion.

## CASE REPORT

An 85-year-old woman presented with a 5×8 mm subcutaneous nodule in the right side of the forehead. The nodule was mobile with respect to the underlying tissue. The woman had 10 years earlier been treated with curettage of a basal cell carcinoma in the hairline, approximately 5 cm above the current location, and the patient was therefore referred to us to rule out recurrence.

The referring dermatologist had taken a biopsy of the overlying skin of the nodule, which only showed actinic keratosis. Thus, the patient was not operated on, but only enrolled in a follow-up program. Four months later, the nodule had increased to 10 mm, and therefore, a new deep biopsy was taken to rule out malignancy. The biopsy still showed no malignancy. The patient continued in the follow-up every 6 months. After 1½ years, the patient had an excisional biopsy, removing the firm nodule. The first histopathology showed a lymph node with me-

*From the Department of Plastic Surgery, Roskilde Hospital, University of Copenhagen, Roskilde, Denmark.*

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tastasis from squamous cell carcinoma. However, because the patient had never had a squamous cell carcinoma, the pathologist did a reassessment of the specimen, which now showed LELCS with massive perineural growth. The tumor was nonencapsulated and subcutaneous, and it infiltrated the underlying muscle tissue. The overlying skin was without malignancy or dysplastic cells. The tumor cells were negative for Epstein-Barr virus (EBV). Furthermore, a reassessment of the earlier removed basal cell carcinoma in the hairline was performed. The diagnosis was confirmed, and no signs of squamous cell carcinoma were found. An examination of the ear, nose, and throat by a specialist showed no sign of tumor.

The patient was treated with reexcision with margins of 1 cm including the fascia. However, a biopsy of a small cutaneous nerve in the margin of the reexcision showed perineural growth, and therefore, the patient was referred to radiation treatment and received 3 GY  $\times$  17 in the operated area including a surrounding margin of 1 cm. The patient currently has finished the radiation treatment and is presently scheduled for clinical follow-up every 4 months for at least 2 years.

## DISCUSSION

LELCS is most often found in the sun-exposed areas of the head,<sup>1</sup> which could suggest a relationship to sunlight exposure. There have also been cases reported on the trunk, arm, and penis.<sup>4,7-9</sup> It often presents as a slowly growing flesh-colored or erythematous firm nodule, papule, or plaque.<sup>1</sup> The tumor normally affects elderly patients, with an almost equal sex ratio.<sup>1,7</sup>

LELCS is a low malignant tumor, with only 2 reported deaths and few cases of extranodal metastases, lymph node metastases, and local recurrence.<sup>1,3,5-8</sup> However, LELCS with perineural invasion is considered a more aggressive tumor.<sup>5</sup> In the English literature, there have been only 2 reported cases of LELCS with perineural invasion. One was treated with Mohs microsurgery, and one was treated with excision, and because of positive margins, received adjuvant radiation and chemotherapy (cisplatin).<sup>2,5</sup> Follow-up showed no recurrence.

Histologically, LELCS is an epithelial neoplasm normally located mainly in the deep dermis, but invasion into subcutaneous fat and sometimes muscle tissue is often occurring.<sup>3,6</sup> LELCS has a dense lymphoid infiltrate but is nonencapsulated, and therefore, it differs from a lymph node. The neoplasm is absent of epidermal and appendageal connections.<sup>3,5</sup> By contrast, squamous cell carcinoma typically is located in the superficial dermis and has connections

with epidermis.<sup>3</sup> As was the case in this patient, some cases of LELCS have an overlying squamous cell carcinoma in situ (actinic keratosis).<sup>4</sup> Historically, LELCS has been speculated to be an adnexal neoplasm,<sup>3,9</sup> but in the new literature, LELCS is classified as a variant of squamous cell carcinoma.<sup>4</sup>

Differential diagnoses include skin metastasis of lymphoepithelioma of the nasopharynx or lymphoepithelioma-like carcinoma of other organs, basal cell carcinoma, squamous cell carcinoma, keratoacanthoma, Merkel cell carcinoma, melanoma, and lymphoma.<sup>1,5</sup>

The only reliable way to histologically differentiate between metastatic lymphoepithelioma of the nasopharynx and LELCS is EBV.<sup>1</sup> Lymphoepithelioma of the nasopharynx is positive for EBV, whereas LELCS is normally negative. There has been only one case reported of EBV-positive LELCS, in a tumor from the cheek of a Japanese woman in whom they found no signs of tumor elsewhere.<sup>7</sup> Metastatic lymphoepithelioma of the nasopharynx to the skin is very rare and often occurs at an advanced stage of the disease.<sup>1,3</sup> However, because lymphoepithelioma of the nasopharynx is an aggressive tumor in contrast to LELCS, it should be ruled out by a simple examination of the nasopharynx.

Lymphoepithelioma-like carcinoma can be found in many organs besides the skin, including salivary glands, oral cavity, thyroid, thymus, trachea, lungs, breast, stomach, biliary tree, intestine, prostate, urinary bladder, uterine cervix, vulva, and vagina.<sup>2,8</sup> Metastasis to the skin should be kept in mind in case of symptoms related to above organs.<sup>1,5,6</sup> Histologically, lymphoepithelioma-like carcinoma is only significantly associated with EBV in the stomach, salivary glands, lungs, and thymus.<sup>2,10</sup>

The recommended treatment of LELCS is excision with a wide surgical margin, a physical examination including an examination of the nasopharynx to exclude lymphoepithelioma of the nasopharynx and EBV testing of the tumor. Radiation therapy should be the treatment where surgery is not an option or in cases with perineural invasion, recurrence, or metastatic disease.<sup>4</sup> Patients should be in a follow-up program after the end of the treatment. Because of LELCS being a variant of squamous cell carcinoma, it should be controlled as such. In case of a palpable tumor, a diagnostic excision should be made removing the entire tumor because, as this case shows, a biopsy of the skin is not sufficient.

## CONCLUSIONS

In conclusion, LELCS is a rare, slow-growing, low malignant tumor with low metastatic risk and recur-

rence even in the more aggressive tumors with perineural invasion. The diagnosis of LELCS is difficult both clinically and histologically, and therefore, a thorough anamnesis and examination is important, including referral to an ENT to rule out metastasis from the more aggressive lymphoepithelioma of the nasopharynx.

**Cecilie Brandt Lassen, MD**

Department of Plastic Surgery  
Roskilde Sygehus  
Køgevej 7-13  
DK-4000 Roskilde  
Denmark  
E-mail: ceciliebl@hotmail.com

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