Lymphoepithelioma-like Carcinoma of the Skin: A Case
Of One Individual Presenting with Two Primary Cutaneous Neoplasms

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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 morphoeform features. The patient also complained of an asymptomatic, slowly enlarging lesion on her left parietal scalp believed to be present for at least three months. Clinical examination revealed a solitary 2.0 x 2.2 cm tan to pink indurated ulcerative plaque (Figure 1). There were no nario-epithelial anomalies or regional lymphadenopathy. A shave biopsy was performed to the left parietal scalp to exclude both basal cell carcinoma and squamous cell carcinoma. The patient’s past medical history was non-contributory and she denied any constitutional symptoms at the time of clinical presentation.

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 invested by a dense lymphocytes infiltrate (Figure 2). The atypical epithelioid cells were basophile 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 membrane antigen (EMA) suggesting tumors of epithelial origin. Staining for CK7 and CK20 yielded negative results excluding Paget’s disease and Merkel cell carcinoma (MCC), respectively, from the differential diagnosis. Due to the concern for an underlying metastatic undifferentiated nasopharyngeal carcinoma or lymphoepithelioma-like carcinoma (LELCS) of another internal organ, an in situ hybridization for Epstein-Barr virus encoded RNA (EBER1/2) was performed for detection of an active or latent EBV infection (Figure 3). The patient’s histologic slides were compared to a control EBER1/2 immunohistochemical stain (Figure 4). The negative EBER1/2 stain for both lesions strongly favors two primary LELCS in our patient and does not favor a metastatic disease related to an EBV-driven undifferentiated nasopharyngeal carcinoma or internal LELCS. Our patient was referred to an oncologist for medical evaluation to exclude a metastasis of an undifferentiated nasopharyngeal carcinoma or lymphoepithelioma-like carcinoma of other internal organs. Given the patient’s advanced age and frail status, the patient refused oncologic examination as she planned to decline systemic treatment if an underlying internal malignancy was discovered. She plans to undergo surgical excision of both cutaneous neoplasms and refrain from systemic therapies which supports the diagnosis of two primary lymphoepithelioma-like carcinomas of the skin.

Discussion

Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare primary cutaneous neoplasm initially described in 1988 by Swanson et al. Since this first report, close to 80 cases have been described in the English literature. LELCS occurs most often in elderly individuals on sun-exposed areas, primarily the head and neck. However, there has been a report of LELCS occurring on the trunk and upper extremities. The incidence occurs equally between men and women. LELCS often presents as a solitary flesh-colored to red, firm papule, plaque, or nodule. The average size is fairly large measuring about 2 to 3 centimeters in diameter. Typically, LELCS is asymptomatic and slowly enlarges over a period of months.

On histology, LELCS presents as a dermal proliferation of atypical polygonal epithelioid cells arranged in nests, cords, or sheets surrounded by a peripheral dense lymphocytes infiltrate. Cellular atypia includes vesicular hyperchromatic nuclei and prominent nucleoli with scant amphophilic to eosinophilic cytoplasm. The reactive lymphoid stroma is comprised of small B- and T-lymphocytes, staining positive for CD19 and CD20, with an occasional plasma cell present. LELCS generally extends into the reticular dermis with occasional involvement into the subcutis and even skeletal muscle. LELCS stains positively for pan cytokeratin, CK5, CK6, p63 and EMA, reactivity likely indicating a neoplastic origin of epithelial cells. In more recent literature, some consider LELCS to be a variant of squamous cell carcinoma (SCC). 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. However, SCC is typically located in the superficial dermis and mantles connectivity with the epidermis. Lastly, others believe that LELCS is a morphologic pattern as opposed to a distinct clinicopathologic entity.

Differential

The differential diagnosis is fairly extensive and includes cutaneous metastasis of undifferentiated nasopharyngeal carcinoma or a lymphoepitheliomas-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 tumors. Histologic features like immunohistochemical staining distinguish LELCS from the possible differential diagnosis.

Figures

Figure 1

Figure 2

Figure 3

Figure 4

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. In addition, peripheral lymphocytic infiltrate is usually absent in MCC. Clarke and Ioffreda report a case in which LELCS demonstrates spindle shaped cells that resemble the spindle cell variant of melanoma. However, unlike LELCS, melanoma is positive for S100 and other neuroendocrine markers such as HMB-45. LELCS can be distinguished from malignant lymphoma by the absence of atypical lymphocytes in LELCS. Epithelial markers such as epithelial membrane antigen and cytokeratin 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 cytokeratin and is positive for CD30 and CD15. Basal cell carcinoma will demonstrate neoplastic basal 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. 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. Cutaneous lymphadenoma demonstrates a similar dense lymphocytic infiltrate as LELCS although these lymphocytes appear benign and monomorphic. Follicular dendritic cell tumor (FDC) is similar to LELCS by way of syncytia-appearing plump cells surrounded by reactive lymphoid cells but FDCT stains negative for cytokeratin markers. FDCt will demonstrate positive reactivity to Ki-M4, CD21, and CD57.

Histologically, LELCS is remarkably similar to metastatic lymphoepitheliomas of the nasopharynx also known as undifferentiated nasopharyngeal carcinoma. Epstein-Barr virus (EBV) reactivity is the main distinguishing factor between LELCS and undifferentiated nasopharyngeal carcinoma. In general, LELCS is negative for EBV reactivity whereas undifferentiated nasopharyngeal carcinoma will test positive for EBV. There has only been one reported case of LELCS in a Japanese woman which tested EBV positive yet no related neoplasms were found elsewhere in her body. In situ hybridization for EBV, the most reliable, specific, and highly sensitive method for detecting latent EBV, was used in this case report and results were negative for EBV in our patient. Metastatic lymphoepithelioma of the nasopharynx is rare, but aggressive when it does occur. LELCS secondary to metastasis of undifferentiated nasopharyngeal carcinoma appears to be very rare as there are less than two cases currently reported in the literature. Nonetheless, it is highly recommended to evaluate the patient for possible undifferentiated nasopharyngeal carcinoma by a complete oncologic exam including indirect laryngoscopy of the nasopharynx. The review of symptoms is recommended when LELCS is confirmed to exclude metastasis from a variety of internal organs.

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. Histologically, EBV reactivity has been associated only with LELCS. The incidence occurs equally between men and women. LELCS has shown the presence of occasional binucleated cells resembling Reed-Sternberg cells, however Hodgkin lymphoma is negative for cytokeratin and is positive for CD30 and CD15. Basal cell carcinoma will demonstrate neoplastic basal 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. 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. Cutaneous lymphadenoma demonstrates a similar dense lymphocytic infiltrate as LELCS although these lymphocytes appear benign and monomorphic. Follicular dendritic cell tumor (FDCT) is similar to LELCS by way of syncytia-appearing plump cells surrounded by reactive lymphoid cells but FDCT stains negative for cytokeratin markers. FDCt will demonstrate positive reactivity to Ki-M4, CD21, and CD57.

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Treatment

For the patients with LELCS, the prognosis is generally good despite its categorization as a poorly differentiated neoplasm. In a large melanoma tumor with rare reports of metastasis to lymph nodes at presentation and to internal organs such as liver, lung, and bone. There are only two reported deaths from metastatic LELCS. There are multiple reports of local recurrence after incomplete excision. Therefore, most LELCS are treated by wide local excision or Mohs micrographic surgery to lower the risk of recurrence. LELCS and undifferentiated nasopharyngeal carcinoma are both radiosensitive and this treatment modality should be considered for recurrent cases, nonsurgical candidates, and those with lymph node metastasis. There are also a few reports of priapial invasion, in which Moehs micrographic surgery, radiation, and chemotherapy were used in combination therapy without evidence of recurrence on follow-up evaluation.

References

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