Lymphoepithelioma-like Carcinoma of the Skin
—Report of a Case—

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Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare tumor with a microscopic resemblance to lymphoepitheliomatous tumors of the nasopharynx. Among the cases reported so far, no clear cancerous cell origin can be found. Some authors suspected adnexal origin because of dermal location of the tumor with focal eccrine, sebaceous, or follicular differentiation. We present an example of this rare cutaneous neoplasm that was located on the nose tip of a 75-year-old man. Histopathologically, the neoplasm has clear connection to the overlying epidermis. To our knowledge, only two cases of LELCS with connection to the overlying epidermis have previously been reported. (Dermatol Sinica 21: 264-267, 2003)

Key words: Lymphoepithelioma-like carcinoma of the skin, Lymphoepitheliomatous tumors of the nasopharynx

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CASE REPORT

In June 1997, a 75-year-old male noted an erythematous, rapidly growing, asymptomatic papule over nose tip for 6 months (Fig. 1). On physical examination, the papule was 0.6 cm in diameter, centrally eroded and had a rolled up border at the periphery without telangiectasia. Patient had no head or neck lymphadenopathy except left side tonsil enlargement. The nasopharyngeal mucosa was free of tumor, too. Multiple enlarged mediastinum lymph nodes and nodular lesions in lung parenchyma were noted on CT scan, which was compatible with a metastatic disease. This patient received wide tumor excision and full thickness skin graft reconstruction as local treatment and local recurrence was not noted. He refused to receive further work-ups and management regarding to his tonsilar and pulmonary metastasis. He expired one and a half years after surgery due to acute renal failure and suspected tumor compression-induced upper airway obstruction.

Histopathology showed a downward expansile tumor with connection to the overlying epidermis (Fig. 2). The tumor had a typical biphasic feature that was consistent with anaplastic, undifferentiated, nonkeratinized cancer cells and heavy lymphoplasmacytic infiltrates (Fig. 3). The cancer cells were polygonal in shape and had eosinophilic cytoplasm. The nuclei were mostly vesicular with one or two conspicuous nucleoli. The cancer cells did not
form cellular strand, or any glandular structure. Instead, they scattered evenly with close conjunction with lymphocytic infiltrates. The inflammatory infiltrates were composed of small lymphocytes and plasma cells. Immunohistochemical studies of cancer cells showed positive reaction for cytokeratin and neuron-specific-enolase. A digoxigenin-labeled 30-base oligonucleotide antisense probe complementary to a portion of the EBV viral transcript EBER1 was used to detect the EBV genome (in-situ hybridization), which failed to find virus infection within the tumor.

DISCUSSION

Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare cutaneous malignancy first described in 1988 by Swanson et al. More than twenty cases have now been reported. This tumor typically presented as a rapidly enlarging, expansile erythematous nodule with or without induration and erosion on the face and scalp. Because of its rapid growth rate, history of having such tumor is typically short. In most reported cases, the duration of the tumor is less than one year. The size of tumor is usually smaller than 3 cm in diameter. Not infrequently, the lesion is initially mistaken for basal cell carcinoma as in our case, or fibroma. The patients range from 50 to 96 years of age and have equal sex distribution. The presented case here shows typical clinical features such as age of onset, duration of disease, tumor size and location. The tumor behavior is not very aggressive since only one metastatic disease had been noted. Although definite tissue proof of metastatic disease in our patient is pending due to patient's refusal, CT scan reveals suspicious metastatic lesions over tonsil, mediastinum nodes and lung parenchyma.

For localized disease, surgery is the standard treatment, either wide tumor excision or Mohs' surgery plus reconstruction. Patients with localized disease carry good prognosis. Most of the reported cases enjoyed long term survival after surgery. Recurrence is encountered in some cases, but it does not affect survival since second operation cured the disease as long as patients were free from metastasis. On the contrary, the case with distant metastasis died 57 months after surgery. It is also the only mortality reported in this disease category. There is still no consensus protocol in the treatment of advanced disease. Several reports advocated the value of post operational radiotherapy. The rationale is that LELCS bears great similarity to NPC histologically, therefore it may be as radiosensitive as NPC. However, due to the rarity of cases, there are not enough experiences to answer whether radiotherapy or chemotherapy should be given as adjuvant therapy. But, for inoperable patients, radiotherapy may be considered to treat these metastatic nodules.

Histologically, LELCS has a characteristic biphasic pattern that resembles undifferentiated nasopharyngeal carcinoma. The tumor is located in mid to deep dermis in most reported cases without connection to overlying epidermis. Tumor cells have vesicular, round to oval, mildly irregular nuclei. They have variable amounts of lightly eosinophilic cytoplasm. The cells may be cohesive to each other with indistinct cell borders to form cellular islands, trabeculae or nodules, but never differentiated to form mature glandular structure or to show obvious keratinization. Cellular atypicality, and mitosis, as a rule, can be found. There is a heavy inflammatory infiltrate in the lesions. The infiltrating cells are composed of small lymphocytes and plasma cells. From immunohistochemical studies published before, the cancer cells are positive for cytokeratin. Neuron specific enolase positive cancer cells can also be found occasionally, as in our case. The infiltrating lymphocytes bear T cell markers. The presenting case has all the typical pathologic features of LELCS mentioned above except its connection to overlying epidermis which makes this case unique from most of the cases reported in the literature. Because of the histological similarity of LELCS to NPC, EB virus had been thought to play a role in oncogenesis of this tumor. But the search for EB virus genome had been negative, both in Caucasian and Chinese patients.
Our patient also showed no EBV genome inside cancer cells. The origin of cancer cells of LELCS remains elusive. An adnexal origin was proposed by some authors due to dermal location and absence of any epidermal connection of LELCS. There are some substantial evidences supporting proposition including eccrine differentiation, focal sebaceous differentiation, trichilemmal keratinization, rudimentary hair papillae, and hair related keratinization.

Only two cases of LELCS with connection to overlying epidermis had been reported. Shek et al. found a focus of epithelial dysplasia in the adjacent epidermis in one case, suggesting that LELCS might have originated from the overlying epidermis. Lind et al. reported one LELCS with apparent origin in the epidermis.

Therefore, we may conclude that lymphoepithelioma-like feature is a nonspecific result of oncogenesis that is shared by both epidermis or adnexal epithelium. Classic adnexa-derived LELCS bears very good prognosis. Metastasis did happen, but only three out of more than twenty cases were reported. There was only one localized, epidermis-derived LELCS reported. Our case here seems to have an aggressive course due to multiple enlarged mediastinum lymph nodes and nodular lesions in lung parenchyma, and he expired one and a half years after the diagnosis.

In summary, this is the second reported case of epidermis-derived LELCS. It is clear histopathologically that the tumor originated from the epidermal keratinocytes. It also provided new evidence in the oncogenesis of the LELCS. Of course, more cases are needed to elucidate its behavior and to determine its optimal treatment protocol.

REFERENCE